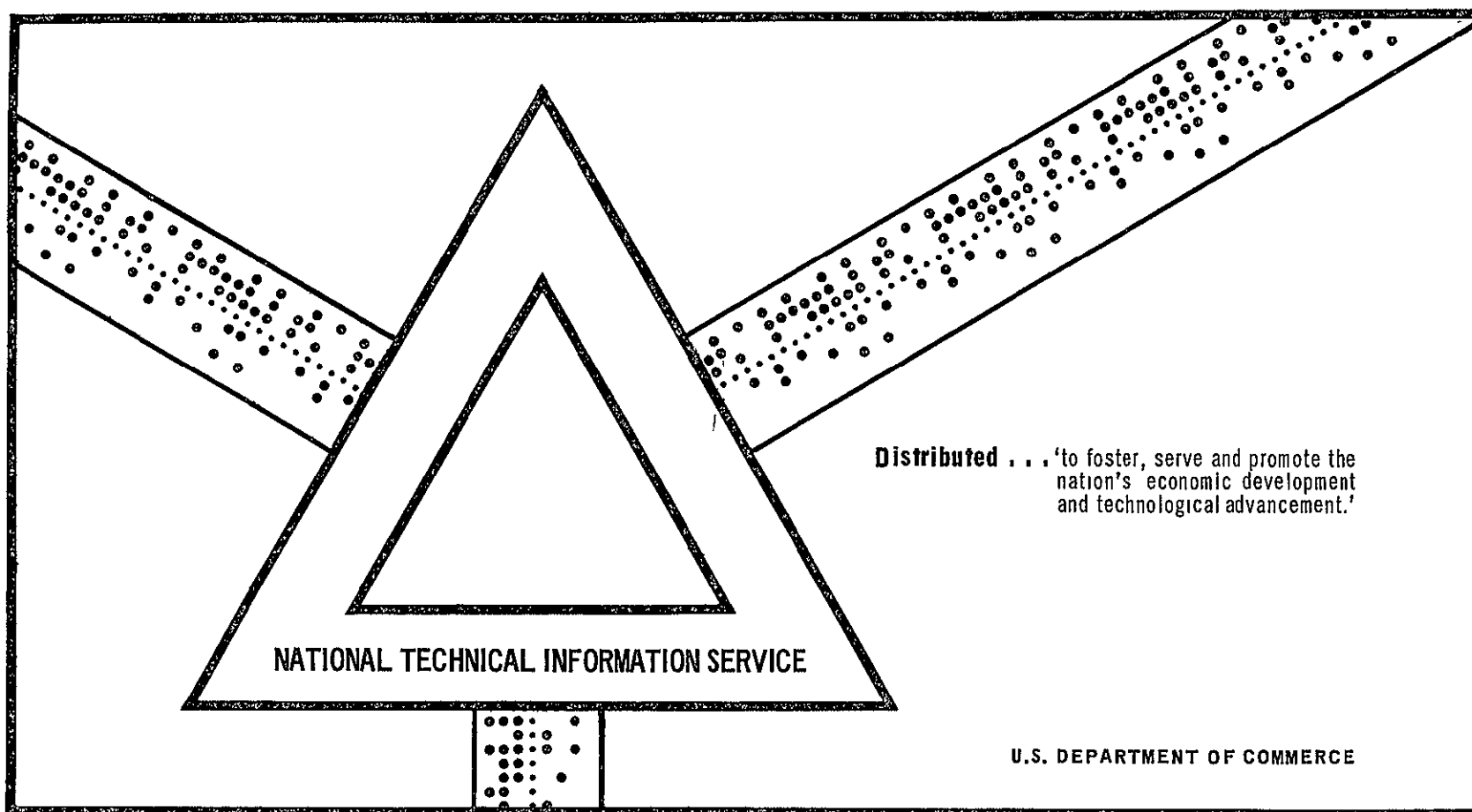


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FLUID BALANCE IN ARTIFICIAL ENVIRONMENTS: ROLE OF ENVIRONMENTAL VARIABLES

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FLUID BALANCE IN ARTIFICIAL  
ENVIRONMENTS: ROLE OF  
ENVIRONMENTAL VARIABLES

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PREFACE

The question of the need for maintaining an adequate humidity in the atmosphere is one that has been of concern to engineers, physicians and physiologists since the first artificial environment was established. While much data have been collected regarding various aspects of the problem, few experiments have been conducted in which the total impact of the environment on crew physiology and comfort have been studied. The research reported here summarizes an extensive series of experiments relating the environment to physiological insensible water loss and crew comfort. The results should be of practical importance in the design of systems requiring humidity control.

The authors wish to express their appreciation to the many individuals in the USAF School of Aerospace Medicine that contributed to the conduct of this study.

B. E. WELCH, Ph.D.

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## LIST OF SYMBOLS<sup>1</sup>

BSA	Body surface area
GC	Atmospheric gas composition
IWL	Insensible water loss
IWL <sub>G</sub>	Metabolic insensible water loss
IWL <sub>R</sub>	Respiratory insensible water loss
IWL <sub>S</sub>	Skin insensible water loss
IWL <sub>T</sub>	Total insensible water loss
P <sub>B</sub>	Barometric pressure
P <sub>H<sub>2</sub>O</sub>	Water vapor pressure
T <sub>a</sub>	Ambient temperature
T <sub>bg</sub>	Black globe temperature
T <sub>ew</sub>	Effective wall temperature
T <sub>s</sub>	Average skin temperature
V	Wind velocity
W <sub>e</sub>	Skin insensible water loss
W <sub>R</sub>	Respiratory water loss
W <sub>Ti</sub>	Light thermal sweating
W <sub>M</sub>	Emotive sweating
W <sub>D</sub>	Diffusional water loss
W <sub>G</sub>	Weight loss through metabolic gas exchange

$W_A$	Initial weight of subject
$W_I$	Total intake (liquid and solid)
$W_O$	Total output (liquid and solid) except $W_e$
$W_Z$	Final weight of subject
$W_{O_2}$	Weight of oxygen in expired air
$W_{CO_2}$	Weight of carbon dioxide in expired air
$W_{ms}$	Weight change on metabolic scale
$W_{ig}$	Weight of water vapor in the inspired gas
$W_{e1}$	Direct measure of skin insensible water loss
$W_{e1t}$	Total skin IWL by direct measurement
$W_{e2t}$	Total skin IWL by indirect measurement
$W_{dr}$	Weight of the Drierite canister
$W_{Rt}$	Total respiratory water loss (in. grams) per experiment
$W_T$	Thermal sweating
$W_{Ts}$	Thermal sweating composed of sensible eccrine activity
$W_{Ti}$	Thermal sweating composed of insensible eccrine activity

<sup>1</sup>Other symbols, applicable only to specific equations, are defined in context.



# FLUID BALANCE IN ARTIFICIAL ENVIRONMENTS: ROLE OF ENVIRONMENTAL VARIABLES

## I. INTRODUCTION

Natural environments which feature extremes of temperature and relative humidity are not unfamiliar to man, although the more remarkable extremes are usually found in desert or arctic climates, where populations are small and dispersed. With the ever-increasing utilization of environmental engineering to provide artificial climates in human habitations and transport vehicles, the specific influence of environmental parameters upon health, comfort, and performance has assumed greater significance. With the ability and technology to control his environment, man must understand the physiologic and metabolic consequences of the microclimates that he has created.

Whereas relative humidities below 25% are rarely experienced for a sustained period in the climate of the temperate zone, indoor heated air may be dried in winter to a relative humidity below 20% day after day. Also, the pressurized cabins of commercial jetliners sometimes produce relative humidities below 10% when the plane has reached cruising altitude. Extremes of dryness have become an accepted part of indoor life--accompanied by a general ignorance or disregard for consequences to health and performance.

In the design of any sealed environmental system--such as an aircraft cabin, spacecraft cabin, or hospital isolation unit--temperature, humidity, wind speed, total barometric pressure, and atmospheric gas composition all play a critical role, not only in human ecology, but also in the satisfactory operation of technical equipment and life-support systems. While excesses of water vapor may condense and freeze on cold valves, oxygen lines, and instrument gages; diminished water vapor pressures may lead to marked discomfort to personnel and unsatisfactory performance levels (121, 123), Excessive temperatures will lead to heavy thermal sweating and an overloading of air-conditioning or life-support systems; while low temperatures will lead to increased metabolic rates, general discomfort, and a significant performance deficit.

Water and thermal balance in artificial environments are, therefore, problems which encompass the full spectrum of human habitats--from the home and office, to the commercial airliner, to the deep-space vehicle. For each of these habitats it is most important to understand the direct influence of each environmental variable upon fluid balance and upon subjective and objective tolerance to the environment.

It is the aim of this paper to investigate the role of the most critical environmental parameters--ambient temperature ( $T_a$ ), water vapor pressure ( $P_{H_2O}$ ), total barometric pressure ( $P_B$ ), wind velocity ( $V$ ), and atmospheric gas composition (GC)--from three

important aspects of human survival and function in artificial environments:

1. Insensible water losses and their skin, respiratory, and metabolic components.
2. Overall fluid and weight balance, and routes of fluid intake and output.
3. Development of signs and symptoms related to environmental intolerance.

Each of these three areas will be explored and discussed in terms of the ambient parameters which most influence them and in terms of their relationships to each other. The possible mediating roles of other environmental or physiologic variables will also be reviewed.

## II. SUMMARY

Considering the results and conclusions of this study, together with the observations and conclusions of other investigators, one may draw the following picture of insensible water loss and of water balance in artificial environments:

1. In the absence of thermal sweating, skin insensible water loss has two significant components:  $W_D$  and  $W_M$ .
2.  $W_D$  results from movement of water in liquid or vapor form through the epidermis, and its rate is dependent upon both the rate of diffusion through the epidermal water barrier and upon the rate of evaporation from the skin. Either step can be rate-limiting.

3.  $W_M$  results from the diffusion and evaporation of water from eccrine and apocrine sweat glands. Most of this water is actively secreted, but some may also diffuse passively from the ducts.

4. From experiments with subjects who are congenitally devoid of sweat glands or who have had them chemically inactivated, it is clear that  $W_D$  is the major component of skin insensible water loss.

5. Five environmental factors---ambient temperature ( $T_a$ ), total barometric pressure ( $P_B$ ), water vapor pressure ( $P_{H_2O}$ ), wind velocity ( $V$ ), and gas composition (GC)--exert a significant influence upon the rate of  $IWL_S$ .

6. The effects of  $P_B$  and of  $P_{H_2O}$  on  $IWL_S$  rates are inversely related over the range studied. There appears to be no interaction between these two variables.

7. The effect of  $T_a$  is directly related to  $IWL_S$  at low  $P_B$ , but not as linear at ground level. There is evidence of a strong interaction between  $T_a$  and  $P_B$  in the determination of  $IWL_S$  rates.

8. The effect of GC on  $IWL_S$  is evident when helium is substituted for nitrogen at 258 mm. Hg  $P_B$ . A significant reduction in  $IWL_S$  rates occurs in the He environment. This reduction may be related to the increased thermal conductivity of He and the resulting increased convective heat loss.

9. The effect of  $V$  is complex and may be mediated by changes in skin temperature and convective heat loss. A direct relationship with rates of  $IWL_S$  exists in the range tested, but at higher values

of  $V$ , the influence of changes in  $P_B$  and  $P_{H_2O}$  are diminished. An interaction between  $V$ , on the one hand, and  $P_B$  and  $P_{H_2O}$ , on the other, is evident.

10. Skin temperature appears to mediate, in part, environmental influences on the rates of skin insensible water loss.  $T_S$  correlates closely with changes in  $T_a$  and with the effective wall temperature ( $T_{ew}$ ).

11. Of all environmental measurements considered, rates of  $IWL_S$  correlated best with  $T_{ew}$ , which provides a determination of the total heat load on a subject.

12. The indirect calculation of  $IWL_S$  ( $W_{e2}$ ) yields results which are consistently higher than those obtained through the direct measurement ( $W_{e1}$ ). The indirect measurement can provide an approximation of skin water losses, but is far from being precise.

13. Intrasubject variation in  $IWL_S$  measurements under identical ambient conditions suggests the possibility of some physiologic regulation of insensible water loss rates.

14. Intersubject variations in  $IWL_S$  rates are also considerable and may be partially related to differences in epidermal architecture and efficiency of the epidermal water barrier.

15. Respiratory insensible water loss is related to the water-holding ability of the inspired air (i.e., the relative humidity) and to the rate and volume of air that passes through the respiratory tract (i.e., the ventilation rate).

16. The effect of  $T_a$  upon  $IWL_R$  is positive but nonlinear, and the effect of  $P_{H_2O}$  is negative and nonlinear.

17. Both  $T_a$  and  $P_{H_2O}$  influence the rate of respiratory water loss by directly altering the R.H. of the inspired air.

18. The effect of  $P_B$  upon  $IWL_R$  is clearly strong and negative. A reduced total pressure lowers the rate of  $IWL_R$  by decreasing pulmonary ventilation.

19. Total insensible water loss is a combination of  $IWL_S$ ,  $IWL_R$ , and  $IWL_G$ , and can amount to over 1,000 gm. in a day, even in a relatively comfortable environment.

20.  $IWL_S$  forms the major component of  $IWL_T$  in all environmental situations tested here and may reach 600 gm./day.

21. Respiratory insensible water loss may contribute up to 44% of  $IWL_T$  in an environment featuring a high  $P_B$  and a low  $P_{H_2O}$ . At reduced  $P_B$  and elevated  $P_{H_2O}$ , this contribution may fall as low as 26%.

22.  $IWL_G$  is relatively constant under the environmental conditions studied here and always formed a very small part of  $IWL_T$ , usually less than 8%.

23. Environmental factors such as  $P_B$ ,  $P_{H_2O}$ , and  $T_a$  all exerted a significant influence upon weight balance and routes of fluid loss even within the "comfort zone."

24. The effect of changes in gas composition on fluid balance was small, but trends were evident.

25. The rate of development and the ultimate severity of signs and symptoms related to the environment are closely dependent upon  $T_a$ ,  $P_{H_2O}$ , and  $P_B$ , with some dependence upon gas composition as well.

26. Signs and symptoms tend to develop more rapidly at reduced  $P_B$  and to reach a more severe level for a given  $T_a$  and  $P_{H_2O}$ . At 700 mm. Hg  $P_B$ , signs and symptoms increased rapidly only below a  $P_{H_2O}$  of 6.5 mm. Hg; while at 258 mm. Hg  $P_B$ , a rapid increase in signs and symptoms occurred below a  $P_{H_2O}$  of 9 mm. Hg.

27. Signs and symptoms are slightly more exaggerated in 100%  $O_2$  and slightly reduced in a He atmosphere, but these changes are not statistically significant.

28. Signs and symptoms develop most rapidly during the first 12 hours of exposure and continue to progress through the first 20 hours of exposure.

29. After the first 20 to 24 hours of exposure, signs and symptoms tended to plateau with no increase in severity and no evidence of improvement. There is no indication of adaptation or acclimatization to the drier environments in the 48 hours of exposure.

30. The nose area showed the most frequent occurrence of symptoms; followed in decreasing frequency-severity by the lip, pharynx, eye, mouth, and tongue areas.

31. The lips exhibited the most frequent development of signs; followed by the eyes, nose, tongue, pharynx, and mouth.

32. Skin, scalp, and general signs and symptoms were least reported and were least severe in exposures no longer than 48 hours.

33. Development of both signs and symptoms in the experimental subjects correlated closely with the rates of skin insensible water loss and total insensible water loss in different environments.

34. Significant variations in skin insensible water loss, respiratory insensible water loss, total insensible water loss, overall weight and fluid balance, and sign and symptom development can be observed when environments within or very close to the accepted "comfort zone," are used. Extreme ambient conditions are not necessary.

35. The qualitative and quantitative analysis of routes of insensible water loss from the human body, as influenced by environmental variables, can be correlated with fluid balance and comfort-performance indices to provide a more complete picture of man's interaction with his environment.

### III. BACKGROUND

Evaporative water losses from the human skin and respiratory tract provide the major mechanism of temperature regulation and heat dissipation in warm environments. In these environments the major component of evaporative water loss is provided by the active secretion of fluid by the sweat glands. The rates of sweat production may reach several liters a day and are dependent upon thermal stimuli acting both centrally (hypothalamic) and peripherally (skin sensors) (7, 8, 11, 12).



Even in environmental situations where sweat glands are not active, however, evaporative water loss from the body surface continues to take place. Observations on subjects congenitally devoid of sweat glands (72, 100, 109), and more recently on subjects whose sweat glands were chemically inactivated (14, 27, 95, 119), have revealed a significant and continuous loss of water through the skin--a loss which is entirely independent of active sweat production. This skin water loss forms a major component of the difficult-to-measure body water loss which was first termed by Sanctorius in 1614 "insensible perspiration" (4). This phrase encompassed nonsweat skin water losses, respiratory water losses, and a small metabolic weight loss created by the slightly excess weight of carbon dioxide exhaled over the weight of oxygen absorbed. Previous measurements have shown that 30 to 40 gm./hr. of water may be vaporized as insensible perspiration, resulting in a heat loss of 20 kcal./hr., or more than 25% of the total body heat loss.

Since the days of Sanctorius many attempts have been made to quantify the components of insensible perspiration and to clarify their relationship to environmental conditions (4, 24, 56, 76, 114, 125). Major difficulties have been created by differences in terminology and in measurement technics, which have often resulted in the accumulation of data which is neither reproducible nor comparable with other experimental results. A reexamination of the phrase "insensible perspiration" points to one of the major problems.

If by "insensible" losses we mean those losses which are not readily observable and are difficult to quantify, then under this category we must place at least five different components (table IB). Each of these components represents material which is lost from the body in a vapor or gaseous state and is, therefore, "not perceptible to the senses." Respiratory water loss ( $W_R$ ) includes the water vapor added to inspired air during respiration and then lost to the environment with expiration. Light thermal sweating ( $W_{T_l}$ ) includes the very low levels of eccrine activity related to temperature regulation which occurs at threshold and does not result in fluid accumulation on the skin surface. Emotive sweating ( $W_M$ ) includes the active secretion from apocrine and eccrine glands on the palms, soles, axillae, and head, which is not related to, nor controlled by, thermal changes. Diffusional, or nonsecretory, water losses ( $W_D$ ) include direct losses through the skin or skin appendages which are nonsecretory in nature. Metabolic gas exchange accounts for the net weight loss ( $W_G$ ) resulting from the excess weight of  $CO_2$  which is expired over the weight of  $O_2$  inspired, or  $W_G = W_{O_2} - W_{CO_2}$ .

Sensible water losses (table IA) include those losses which are easily observed and measured because they occur in the liquid phase: urine, feces, vomitus, drooling, tearing, and significant thermal sweating. This categorization of water losses is a most useful one because it includes all normal types and also provides a practical differentiation of routes and underlying control mechanisms.

All varieties of insensible water loss would have to be included in a discussion of difficult-to-measure water losses (table IC), but the two groups cannot be considered synonymous because of the partition of thermal sweating into both the "insensible" and the "sensible" water-loss categories.

The determination of the rates of total insensible water loss and its components is largely dependent upon the technics of measurement. If a skin-capsule method is used to determine skin water loss, then only the  $W_D$  component (assuming no thermal sweating) is measured if the capsule is placed on the abdomen or back, or the  $W_D$  plus the  $W_M$  components if the capsule is placed on the palm or forehead. Using this capsule technic, one can only roughly extrapolate the actual total-body skin water loss from data derived from localized areas. In the same way the localized measurements of skin water loss rates are difficult to relate to a determination of total insensible water loss.

Using the whole-body gravimetric technic, however, one is immediately provided with a summation of all routes of insensible weight loss including  $W_D$ ,  $W_M$ ,  $W_G$ , and  $W_R$  (fig. 1). By collecting and measuring  $W_R$  and  $W_G$ , one can then determine the actual total-body rate of skin water loss ( $W_e$ ) and isolate all the components of  $IWL_T$ . While this technic is most suitable for obtaining a picture of the rates of total insensible water loss with its skin ( $IWL_G$ ), respiratory ( $IWL_R$ ), and metabolic ( $IWL_G$ ) segments (fig. 1), it provides no information concerning regional variations in water loss rates.

Because the objectives of this investigation are related to overall water balance in artificial environments and to the interaction of ambient variables with rates of sensible and insensible water losses, the whole-body gravimetric technic, was selected over the capsule procedure. In addition to the direct measurement of skin insensible water loss, a derived or indirect calculation of this loss, utilizing a complete weight-balance equation, was also undertaken (see table IC and Methods).

Of all the categories of difficult-to-measure water losses, skin insensible water loss has been the most formidable in terms of direct and accurate measurement and in terms of the determination of the exact mechanisms involved (32). Previous measurements of IWLs have involved more than two dozen separate investigators, multiple anatomical sites, and at least seven different experimental techniques (table II).

Beginning with Ikeuchi's whole-body gravimetric measurements in 1927 (62) and progressing to Goodman and Wolf's infrared airflow analysis studies of 1969 (50), measured rates of IWLs have ranged from 1.5 (103) to 90.0 gm./m:<sup>2</sup>/hr. (83), a span of over 60-fold.

Earlier experimental data on skin water loss, such as the work of Taylor and Marbarger (112), demonstrated a partial dependence of water loss upon some environmental variables, especially humidity and air movement. Further studies by Buettner (24), Hale et al. (56), Hertzman et al. (60), and others (28, 76, 113) showed

variations in water loss rate dependent upon humidity, airflow, temperature, and barometric pressure. However, the direction of these variations and their degree continued to generate disagreement in the literature. As an example, reduced barometric pressure was found by Foa (as cited in Marshall and Specht, 75) and by Guillemard et al. (55) to produce a decrease in skin insensible water loss, while Pi-Suner (98) concluded that reduced  $P_B$  had no effect, and Hale et al. (56) and McCutchan and Taylor (76) agreed that reduced  $P_B$  significantly increased the rate of IWL<sub>G</sub>.

The measurement of IWL<sub>R</sub> and of IWL<sub>G</sub> has been subject to much less controversy and most investigators have reached general agreement about the rates of water loss and the influence of some environmental variables upon these rates (19, 28, 29, 75, 131).

The direct effects of some environmental variables upon human fluid balance are quite apparent. Large increases in ambient temperature lead to increased evaporative water losses by sweating. Although renal fluid output diminishes as a compensatory measure, water conservation is usually not sufficient to maintain fluid balance, and an increased fluid intake must take place.

Much more subtle alterations in fluid balance may be caused by other environmental alterations, such as changes in  $P_B$ . In 1961, Welch et al. (126) observed that experimental subjects living in a space-cabin simulator, with  $P_B$  reduced first to 383 mm. Hg and then to 189 mm. Hg, lost considerable weight (an average of 3.25 kg. in 30 days)

and that this weight loss was accompanied by a considerable loss of total body water. With the advent of manned spaceflight, the combination of reduced barometric pressure, increased oxygen tension, and weightlessness was found to produce significant losses in total body fluid, with fluid loss failing to act as a stimulus for increased fluid intake (47, 48).

In determining 24-hour fluid balance under a wide variety of environmental conditions, all sources of intake and output must be carefully measured. Utilizing a general balance equation (table IC), one can determine  $IWL_S$  by an indirect method in which one solves for  $W_e$  in the balance equation.

When considering the total fluid output in the 24-hour balance studies, one can look at the contribution of total insensible water loss to the total output and examine the influence of the various environmental parameters in increasing or decreasing this contribution. In a similar manner, one can break down  $IWL_T$  into its components of  $IWL_S$ ,  $IWL_R$ , and  $IWL_G$  and examine the relative importance of each of these when environmental conditions are varied. Although it has been stated that  $IWL_S$  is the greatest contributor to  $IWL_T$  (4), it is not clear that this dominance holds for all normally encountered ambient conditions.

The effect of varying environmental parameters upon human health, comfort, and performance has been the subject of serious investigation since 1775 when Blagden (15) studied the effects of

very hot, dry air on human subjects. Since that time it has been recognized that many ambient parameters--such as water vapor pressure (4, 8, 56, 114), wind speed (109, 113), temperature (24, 44, 113), atmospheric gas composition (40, 59, 127), and total pressure (40, 56, 76)--can directly influence comfort, and that the interaction of these parameters can profoundly influence the rate of onset of signs and symptoms of environmental intolerance (101).

Extremes of ambient temperature will lead to profuse sweating and inordinate fluid loss on the one hand, and to shivering and increased metabolic rate on the other. In either case, performance will diminish. The conventional ASHRAE human-comfort guidelines (2), applicable to subjects sitting still in light clothing, suggest a comfort zone of dry-bulb temperature of 71° to 82° F. This comfort zone is modified only slightly by changes in wet-bulb temperature or relative humidity, so that the ideal comfort temperature is defined as 77° F. with a 30% R.H., and 76° F. with a 90% R.H.

Such comfort guidelines have tended to obscure the importance of water vapor pressure in the environment. Whereas very high  $P_{H_2O}$  will effectively prevent adequate human heat dissipation through evaporation and lead to accumulations of water on skin and clothing, very low  $P_{H_2O}$  will lead to localized discomfort and impairment of the sensorium (74). The effects of low humidity are primarily localized to those areas directly exposed to the ambient conditions and not protected by keratinized epidermis or epidermal appendages.

Drying of mucous membranes of the nose, mouth, and pharynx is common and is often followed by inflammation. Chapping of the lips is one of the earliest signs of drying, while drying of the eyes can become a serious medical problem, with the development of conjunctivitis, pain, and diminished vision. Skin and scalp drying, with resulting itching and flaking, also present a major problem.

Morning nasal stuffiness during the winter months is a problem familiar to most inhabitants of the temperate zone, and humidifiers have seen increasing use in an attempt to ameliorate this discomfort. American astronauts in the Mercury, Gemini, and Apollo programs have repeatedly complained of nasal stuffiness, mouth dryness, and lip-chapping in their low-humidity environments (85). In this situation, the contributing effects of low barometric pressure and high oxygen tensions must also be considered.

Wind velocity will affect comfort by changing the rates of convective heat transfer and by altering the rate of water evaporation from the human skin (34, 39). Elevated wind velocities will lead to subjective cooling and to increased drying of exposed surfaces.

Gas composition will also affect comfort by altering the heat capacity and thermal conductivity of the surrounding medium. Helium, for example, will be more efficient than nitrogen in removing body heat and will cause greater human heat loss to the environment (13, 40).

Total barometric pressure will influence comfort by altering convective and conductive heat losses and may also change the rates of



insensible water loss and body heat loss through evaporation (30, 81). Therefore, reduced barometric pressures may augment the rates of insensible water loss and lead to signs and symptoms of drying at water vapor levels significantly higher than those levels which might cause symptoms at sea level.

#### IV. METHODS AND PROCEDURES

Environmental studies were conducted in the altitude-chamber complex located in the Environmental Systems Division of the USAF School of Aerospace Medicine, Brooks AFB, Tex. The facility is composed of two pressure chambers--a laboratory area of 58 m.<sup>3</sup>, and a living area of 28 m.<sup>3</sup>--connected by two air locks (fig. 2). Separate environmental control systems serve each section and provide accurate regulation of ambient temperature, water vapor pressure, total barometric pressure, and gas composition. Wind velocities could be regulated above baseline values only in the laboratory section, through utilization of a specially constructed and damped fan bank.

Although subjects spent approximately equal amounts of time in both the laboratory and the living area during an experiment, all measurements of insensible water losses by the gravimetric method were conducted in the laboratory section, where environmental parameters and subject data were closely monitored. During chamber operation ambient conditions were monitored by four specially trained personnel, two for each section, while all subject data as well as chamber-parameter readouts were supervised by an experiment coordinator.

During measurements of skin insensible water losses, 20 channels of data were collected, displayed, and sampled automatically at 15-second intervals by a digital data acquisition system (VIDAT); all data were stored on digital tape and later tabulated and summarized by computer program. A backup system of analog-tape recording was also utilized, and this system served as the primary system for acquisition of ECG, heart rate, respiratory waveform, and respiratory rates. All data were also recorded manually at 15-minute intervals to provide a further backup and a check of computer accuracy.

The 20 channels of recorded data are listed in table III; also shown are the symbols utilized to denote each parameter and the accuracy of measurement of each channel. All data channels were recalibrated daily. The arrangement of data sensors in relation to the experimental subject is shown in figure 3.

In addition to the 20 parameters directly measured, two temperatures were computed from the telemetry data (table III). These were the average skin temperature ( $T_s$ ) and the effective wall temperature ( $T_{ew}$ ), both of which will be discussed herein.

The seven skin temperatures were monitored by disc thermistors fixed in a thin perforated Teflon harness. The harness insured that the thermistors would be placed in the same location with equal amounts of pressure against the skin during each measurement. An average skin temperature was calculated by using the area weighting coefficients of Du Bois and Du Bois (38). Rectal temperatures were

measured by a Teflon covered thermistor probe, while black-globe and ambient temperature thermistors were placed in a location fixed with respect to the experimental subject. Thermistor probes were repeatedly checked against calibrated water baths.

The effective wall temperature ( $T_{ew}$ ) was computed by using a number of constants, factors, and parameters, including the black-globe temperature, the ambient temperature, and the subject average skin temperature.  $T_{ew}$  reflected the total effective radiative heat load on the experimental subjects (116, 118) and could, therefore, correlate with rates of skin insensible water loss.

$$*T_{ew} \approx \left[ \frac{h(T_{bg}-T_a) + \epsilon \sigma F_{bg-s} \left[ (T_{bg}+273)^4 - (T_s+273)^4 \right] + (T_{bg}+273)^4}{F_{bg-w}} \right]^{1/4} - 273 \quad (1)$$

$h$  Heat transfer coefficient

$\sigma$  Boltzmann constant

$\epsilon$  Black-globe emittance

$F_{bg-s}$  Geometric view factor (globe-subject)

$F_{bg-w}$  Geometric view factor (globe-surroundings)

Water vapor pressure was measured with a Cambridge thermoelectric dewpoint hygrometer, while total barometric pressure was read by a Wallace and Tiernan bourdon tube apparatus. Gas partial pressures were determined by automatic analyzers (oxygen, by a Beckman F3 paramagnetic analyzer; nitrogen, by a Med-Science Electronics Nitralizer; and carbon dioxide, by a Beckman infrared analyzer). Wind

velocities were measured with an Anemotherm warm-wire anemometer with the velocity probe fixed in relationship to the subjects.

The Electrocardiogram was picked up by two electrodes placed on the chest, and heart rate was derived from the QRS frequency. Respiratory waveforms were reproduced by a sensitive thermistor implanted in the outflow track of the face mask, and respiratory rates were derived by counting the peaks of this waveform.

The rates of skin insensible water loss were determined gravimetrically on a total-body basis through the use of a hydraulic metabolic balance manufactured by the Brookline Instrument Company (as described in Bradhma et al., 18). The original balance was specially adapted for this experiment by several modifications: automatic temperature compensation was introduced; a nonflammable hydraulic fluid (Fluorolubes) was installed; special electronic damping circuits were connected to the scale output; and a steel mesh weighing platform was built. The scale was sensitive to weight changes of  $\pm 1$  gm. with a load in excess of 150,000 gm. The scale output consisted of a variable voltage which was fed both to a Honeywell strip-chart recorder and to computer tape through the VIDAT. A weight change of 40 gm. produced a voltage change of 50 mv., or 1.25 mv./gm. The scale was also calibrated daily with the use of a set of removable 5- and 10-gm. weights. The scale was found to maintain its zero point and its sensitivity without drift. The weight-change records were analyzed to determine the average rate of weight loss (gm./hr.) during each

experiment. The true rates of skin IWL were calculated by the formula discussed below.

During measurements of weight loss, respiratory water was trapped in a face mask, hose, and Drierite (anhydrous  $\text{CaSO}_4$ ) canister system. Environmental chamber air of known temperature and water vapor content was inspired directly into the face mask, and all expired air was passed into well-baffled steel canisters packed with measured amounts of indicator Drierite. Approximately 1,600 gm. of the drying material were placed in each canister before a weight measurement was made on the metabolic scale. The canisters plus Drierite were weighed to  $\pm 0.1$  gm. before each subject run and then fixed to the metabolic scale. After each run the gain in weight of the canister and its hose was measured, and the weight change in grams per hour was computed. Since the canister and hose were fixed to the scale, the water vapor trapped (consisting of both water vapor of the inspired air and water vapor added by the respiratory tract) was continuously subtracted from the overall measurement of insensible weight loss by the metabolic scale.

Theoretical considerations (57) would predict that 1,600 gm. of Drierite could extract all but 0.005 mg./liter of water from an air-stream moving at a rate of 550 liters/hr. Such efficiency would mean that all but 0.1% of the total expired water vapor would be trapped in the cylinders if airflow were less than 550 liters/hr. Since each canister was used for a maximum of 40 minutes before the Drierite was

changed, the canisters would absorb a maximum of 15 gm. of water vapor in that time (assuming 88% saturation). The canisters would be capable of absorbing 135 gm., however--meaning that they never were loaded with more than 11% of their maximum absorptive capacity (35, 57).

In actual practice it was found that a color-indicator change involved less than 25% of canister Drierite at the end of a 40-minute run. Repeated measurements of canister efficiency demonstrated that a minimum of 97% of the expired water vapor was trapped in the canisters. During all calculations, therefore, it was assumed that all expired water had been trapped.

#### Experimental subjects

Seven volunteer subjects were selected from a large group of basic trainees at Lackland AFB, Tex. The subjects, all male Caucasians between the ages of 18 and 20, were thoroughly evaluated as to state of health, and personal and family history; all passed the Class III Flying physical examination. Pulmonary, hematologic, renal-electrolyte, and thyroid functions were found to be within normal limits (table IV). No physical evidence or history of sweating abnormalities or temperature intolerance could be elicited. Five of the subjects served throughout the 81-day experimental program, while subject P.K. was substituted for subject K.F. early in the project because of a personal problem. Subjects were identified by letters from "A" to "F" throughout the study with subjects A, B, and C forming the first experimental group, and subjects D, E, and F forming

the second group. Six subjects were utilized in experiments lasting 24 hours or longer.

### Clothing

To provide a maximum surface for free evaporation, all subjects wore only abbreviated loincloths made of Beta cloth and fastened with a tie of the same material. Beta cloth was utilized because of its nonflammability in enriched oxygen environments. The only other articles of apparel permitted were standard rubber bathroom thongs which were open across the top and sides. These thongs were always removed during measurements of weight loss on the metabolic scale.

### Project outline

Experiments were conducted over an 81-day period. Table V illustrates the general plan of insensible weight loss experiments during this time. An initial control period of 10 days consisted of three 48-hour experiments at 700 mm. Hg  $P_B$ , 14 mm. Hg  $P_{H_2O}$ , and low wind velocities. Ambient temperature was varied from 20° to 28° C.

The experimental period was divided into four parts--the first lasting 21 days and conducted at 700 mm. Hg  $P_B$ . Varying combinations of  $P_{H_2O}$ ,  $T_a$ , and  $V$  were investigated. The second part, also running 21 days, duplicated the experimental conditions of the first, except for a total pressure of 258 mm. Hg. The third part, running for 13 days, was also conducted at 258 mm. Hg  $P_B$  but utilized varying gas compositions--specifically, 100% oxygen and a mixture of oxygen and helium--as well as varied  $P_{H_2O}$ . The fourth experimental period spanned 6 days and was run at the intermediate  $P_B$  of 480 mm. Hg.

A final control period of 10 days terminated the project and consisted of repeat experiments at 700 mm. Hg  $P_B$ , at varying temperatures and water vapor pressures. A single experiment of 565 mm. Hg  $P_B$  and very low  $P_{H_2O}$  was also completed to simulate environmental conditions aboard an Air Force medical evacuation aircraft.

A complete listing of the 38 individual experiments, as well as the duration and ambient conditions of each, is given in table VI. Each experiment is identified by a number-letter code; the former denoting the project period and part (table V); and the latter, the specific environmental parameters.

Each experiment varied in duration from 10 to 48 hours. Complete fluid- and weight-balance studies were accomplished only on experiments lasting 24 hours or longer. The shorter experiments involved stepwise changes in water vapor pressure, with all other conditions held constant. During the study subjects were placed on a controlled diet of dehydrated freeze-dried foods of known composition which were rehydrated with measured amounts of fluid just before consumption. The same diet was served throughout the study (table VII) and calculated to keep the subjects at a relatively constant weight (table VIII). Accurate and complete monitoring of all solid and liquid intake could be achieved. During an experiment subjects were allowed free access to water, but all intakes were carefully measured and recorded. All urine and feces outputs were collected for analysis of solid and liquid components.



### Experimental protocol

A period ranging from 24 to 48 hours was provided between experiments to allow the environmental chambers to equilibrate to a new set of conditions and to allow the experimental subjects to recover from any signs or symptoms which might have developed during the previous experiment.

Four hours before each study, subjects were carefully examined by a physician; subjects then examined one another according to a protocol to be described further on. Subjects next underwent 3 full hours of 100% oxygen prebreathing. The oxygen was saturated to between 85% and 95% with water vapor to prevent drying of mucous membranes. Since 180 minutes of oxygen prebreathing would be required to prevent bends development at the higher altitudes studied (i.e., 258 mm.-Hg  $P_B$ , or 27,000 ft.), it was decided to institute a uniform prebreathing program for every experiment regardless of  $P_B$ . Subjects examined immediately after this prebreathing program showed no new physical signs or symptoms that could be attributed to this experience.

After completion of prebreathing, subjects dressed in Beta cloth loincloths and thongs. Half of the experimental subjects (A, B, and C) then entered the laboratory section of the environmental complex through the airlock. Total-body weights were obtained for each subject on the metabolic scale.

A typical plan of a 24-hour experiment is shown in figure 4. After an hour of equilibration within the chamber, each of the subjects

underwent the first measurement of insensible water loss rates on the metabolic scale. The subject was connected to the Teflon harness, to all sensors, and to the mask-Drierite system. After a few minutes of equilibration during which time the scale was zeroed, an actual weight measurement period of precisely 30 minutes was initiated. During this 30-minute period all 20 channels of data were recorded both manually and on computer tape. At the precise termination of the period, all data acquisition was ended and the Drierite canister disconnected and reweighed.

After the first group of subjects had completed the initial measurements of IWL rates, they moved into the living area of the environmental complex, where they ate and then slept. The second group of subjects (D, E, and F) then entered the laboratory section, where total body weights and rates of IWL were determined. During the remainder of the experiment, the two groups of subjects exchanged places several times; while one group underwent weight measurements in the laboratory, the other ate or slept in the living area.

Throughout the study, each subject evaluated himself for symptoms of discomfort at fixed intervals and also evaluated other subjects for sign development. All subjects were allowed only mild activity and were provided with television, radio, checkers, chess, and limited reading material. Approximately 35% of the total experiment time was provided for sleep, and subjects were given three meals in a 24-hour period. During the 48-hour experiments

each of the 6 subjects underwent IWL rate measurement four times; and during the 24-hour experiments, three times. During the shorter 10-hour studies, only 3 subjects were used, and each underwent two IWL determinations. At the conclusion of each experiment every subject again underwent a total-body-weight determination, and the net gain or loss of weight during the study was calculated.

#### Measurement of skin IWL ( $W_{e1}$ )

The rate of skin insensible water loss was calculated utilizing the rate of weight loss per hour as measured on the metabolic scale. This observed rate of weight loss did not provide a true measure of skin IWL, however, for two reasons. First, the Drierite canister which is fixed to the scale collects not only water added to the expired air by the respiratory tract but also water vapor contained in the inspired air. The weight of this amount of inspired water vapor can be easily estimated, however, if the precise ambient conditions are known and the pulmonary ventilation of each subject under those particular ambient conditions has been measured (table IX). Expired gas volumes were measured with a Tissot spirometer, corrected to ambient parameters, and then used to closely estimate pulmonary ventilation and the amount of water added to the canisters by the inspired air.

The second factor which must be considered relates to the insensible weight loss due to metabolic gas exchange: i.e., that weight of  $CO_2$  expired which exceeds the weight of  $O_2$  absorbed. This weight loss ( $IWL_G$ ) forms part of the weight loss measured by the metabolic

scale and, thus, must be corrected for. Rates of gas exchange were determined for all subjects while on the experimental diet and at complete rest (table X). Oxygen and carbon dioxide content of expired air were measured with a Beckman F<sub>3</sub> paramagnetic analyzer and a Beckman infrared analyzer, respectively. Respiratory quotients and  $W_{O_2} - W_{CO_2}$  values were measured from 20° to 28° C. T<sub>a</sub>, and these values were utilized in determining the rates of true skin IWL ( $W_{e_1}$ ) with the following formula:

$$W_{e_1} = W_{ms} + W_{ig} - W_G \quad (2)$$

where:

$W_{e_1}$  is the direct measurement of skin insensible water loss (gm./hr);

$W_{ms}$  is the weight change on the metabolic scale (gm./hr);

$W_{ig}$  is the weight of water vapor in the inspired gas (gm./hr.); and

$W_G$  is the IWL due to metabolic gas exchange (gm./hr.).

Values for  $W_{e_1}$  were finally divided by the BSA measurements of each experimental subject (table IV), so that all IWL<sub>S</sub> rates could be expressed as grams per square meter per hour. Since skin insensible water loss rates clearly depend upon skin surface areas, the expression of  $W_{e_1}$  in grams per square meter per hour makes the data from differing environmental situations more directly comparable and negates major differences in subject size. Values of  $W_{e_{1t}}$  in terms of total grams per experiment were also computed by use of the formula:

$$W_{el_t} = W_{e_l} \times BSA \times \text{Duration} \quad (3)$$

where:

$W_{el_t}$  is the total average skin IWL per experiment (gm.);  
 $W_{e_l}$  is the average skin IWL (in gm./m.<sup>2</sup>/hr.);  
 BSA is the body surface area of the subject (m.<sup>2</sup>); and  
 Duration is the length of the experiment (hr.).

#### Measurement of respiratory water loss ( $W_R$ )

Water in the expired air was trapped in the Drierite-canister system and weighed to  $\pm 0.1$  gm. after each determination of skin IWL. This weight change, however, also represented the weight of water carried in the inspired air, as well, as water added by the respiratory system. To obtain the true rate of respiratory insensible water loss ( $IWL_R$ ), the weight of the water in the inspired air must be subtracted from the total canister weight change. This weight of inspired air water ( $W_{ig}$ ) was discussed previously in the measurement of skin IWL. The determination of  $IWL_R$ , or  $W_R$ , then becomes:

$$W_R = W_{dr} - W_{ig} \quad (4)$$

where:

$W_R$  is the respiratory insensible weight loss (gm./hr.);  
 $W_{dr}$  is the weight change of Drierite canister (gm./hr.); and  
 $W_{ig}$  is the weight of water vapor in the inspired air (gm./hr.).

Values for  $W_R$  were also expressed in grams per square meter per hour so that major differences in subject size could be negated. A  $W_{R_t}$  value

in terms of total grams per experiment was computed in the same manner as the  $W_{e1_t}$  value discussed above.

#### Measurement of total insensible water loss ( $IWL_T$ )

The total IWL is composed of skin insensible water loss ( $IWL_G$ ), as measured by  $W_{e1}$ ; of respiratory insensible water loss ( $IWL_R$ ), as measured by  $W_R$ ; and of metabolic insensible weight loss ( $IWL_G$ ), as measured by  $W_{O_2} - W_{CO_2}$ .

Therefore:

$$IWL_T = W_{e1} + W_R + W_G \quad (5)$$

Values for  $IWL_T$  were finally expressed in grams per square meter per hour, as were  $W_{e1}$  and  $W_R$ --to negate major differences in subject size. An  $IWL_T$  value in terms of total grams per 24 hours was also derived so that total amounts of insensible water loss per day could be compared under varying environmental conditions.

#### Fluid balance studies

In all experiments of 24- and 48-hour duration, careful weight- and fluid-balance studies were conducted. All intakes and outputs were measured and tabulated for each subject. In addition, precise initial and final weighings ( $\pm 1$  gm.) on the metabolic scale were carried out. From these data an indirect calculation of skin insensible water loss ( $W_{e2}$ ) was derived by use of the complete weight balance formulas shown in table IC. In the final analysis:

$$W_{e2} = W_A - W_Z + W_I - W_O + (W_{O_2} - W_{CO_2}) \quad (6)$$

In this case,  $W_{O_2} - W_{CO_2}$  is not comparable to the  $W_G$  values discussed above, since average metabolic activity during the entire experiment is considerably higher than the basal activity measured when the subject is lying on the metabolic scale. Table XI shows the values for  $W_{O_2} - W_{CO_2}$  based on an average estimated oxygen consumption of 25 liters/hr. as compared with a basal level of 16 liters/hr. These values were used in calculating  $W_{e_2}$  by the above formula. The values obtained for  $W_{e_2}$  (gm./experiment) were then expressed as  $W_{e_{2t}}$  (gm./24 hr) and compared with the values obtained for  $W_{e_{1t}}$  (gm./24 hr.). Other fluid balance terms are defined in table IIC. In all studies, data from participating subjects were averaged to give a single mean value per experiment.

#### Sign and symptom evaluations

Throughout all studies, but with special emphasis on the 24- and 48-hour experiments, evaluation of signs and symptoms related to environmental conditions was carried out. These evaluations consisted of several parts.

Before subjects entered the chambers to commence an experiment, they received a physical examination by a physician. This examination was repeated when subjects left the chambers at the conclusion of an experiment. The physician filled out an Objective Evaluation Sheet on each subject at these times (table XII). In addition to evaluating the eight anatomical areas listed on the sheet, he was required to provide an overall impression of the well-being of the subject and to

list other abnormal signs that he might find. He also administered several sensory tests including a Schirmer test, near and distant visual acuity test, olfactometry, and gustometry. These tests will subsequently be discussed in detail.

All of the experimental subjects were trained to evaluate their own symptoms and to detect and evaluate signs in other subjects. Before the studies began they were given a course of instruction by the Ophthalmology and Otolaryngology Departments of the USAF School of Aerospace Medicine. In this course they were familiarized with the signs and symptoms which might develop under adverse ambient conditions and were given practice in evaluating and grading them by use of subjective and objective evaluation sheets which were provided (table XII). Subjects were also instructed on the technics of performing Schirmer's test and visual acuity tests within the chambers.

Before each experiment, a subject would evaluate himself by the Subjective Evaluation Sheet and would then evaluate a specific partner with the Objective Evaluation Sheet. Upon entering the chamber and at specific intervals throughout the study, these subjective and objective evaluations would be carried out. The subjects made final evaluations immediately upon leaving the chamber.

During the first 8 hours of an experiment, subjective evaluations were conducted hourly and objective evaluations every 2 hours. After 8 hours, subjective evaluations were conducted at 2-hour intervals and



objective evaluations at 4-hour intervals (except when subjects were sleeping). Evaluations were usually programmed to occur both immediately before and immediately after a sleep period. Visual acuity and Schirmer tests were conducted at 8-hour intervals.

A subjective frequency-severity index was derived to describe sign development quantitatively, and an objective frequency-severity index derived to describe symptom development. These indices depended upon the difference in magnitude between a sign or symptom level originally reported in an anatomical category (i.e., "Eyes") and the highest level subsequently reported in that category. If a subject initially noted a "1" in a category, but later reported a "3", the difference was then tabulated as "-2". For each anatomical category the changes or differences were averaged for the subjects involved. The anatomical averages were then added together and divided by the number of anatomical categories (always 10) to give an overall average. This average represented the sign or symptom index value. „

$$\text{Index number} = \frac{\sum_{n=1}^{10} \left[ \frac{\sum_{i=1}^{n_s} (x_{i_o} - x_{i_m})}{n_s} \right] n}{10} \quad (7)$$

where:

$x_{i_0}$  = Initial value

$x_{i_m}$  = Maximally changed value

$n_s$  = Number of subjects

$n$  = Anatomical categories (1-10)

$i$  = Subjects ( $1 \rightarrow n_s$ )

For each experiment three initial indices were derived: a physician objective evaluation, a subject objective evaluation, and a subject subjective evaluation. The first two of these were averaged to provide an overall Sign Frequency-Severity Index, while the third stood alone as the Symptom Frequency-Severity Index. The three averaged together formed the Sign-Symptom Index.

The relative frequency and severity of signs and symptoms by anatomical region were derived by looking only at the regional averages:

$$\left[ \frac{\sum_{i=1}^{n_s} (x_{i_0} - x_{i_m})}{n_s} \right] \quad (8)$$

The time course of sign and symptom development was derived by measuring the change in sign or symptom severity with respect to time

rather than looking at the maximum change. The formula then became:

$$\sum_{n=1}^{10} \left[ \frac{\sum_{i=1}^{n_s} (x_{i_0} - x_{i_t})}{n_s} \right]_n \quad (9)$$

10

where:

$x_{i_0}$  = Initial sign or symptom value

$x_{i_t}$  = Value at specific point in time (1 to 48 hours)

Since in all the indices the maximum or time-dependent value was subtracted from the initial value, the sign or symptom index would have a value of "zero"-if there were no change in any subject in any anatomical area during an experiment. As signs or symptoms became more severe, the indices would become increasingly negative in value, and if signs or symptoms actually improved during an experiment, the indices would have a positive value.

#### Other sensory tests

1. Schirmer's test. Small strips of filter paper (No. 42) measuring 30 mm. by 5 mm. are folded to form a 4-mm. hook on one end. This hook is then carefully placed over the lower eyelid so that it is in contact with the palpebral conjunctivum, and the eye is closed. After 120 seconds, the strip is removed from the eye and a measurement is made of the amount of the strip that has become wet; i.e., somewhere between 0 and 30 mm. Although the presence of the

strip against the conjunctivum initially acted as a foreign body to induce excessive tearing, it was found that subjects quickly accommodated to the procedure. After several weeks of practice, the strips could be readily introduced without any initial tearing. This test was performed before chamber entry and again immediately upon exiting. The difference in wet length between the initial and final measurement ( $L_i - L_f$ ) was used as the increment of Schirmer change.

2. Visual Acuity. Both near and distant visual acuity were tested at varying times before, during, and immediately after an experiment. Standard 20-ft. acuity charts for distant vision and reading cards for close acuity were utilized. Any alteration in the smallest type that could be read was noted as a change in acuity, with a value of  $-1$  given for each line of larger type and a value of  $+1$  for each line of smaller type that the subject was forced to accept as threshold.

3. Gustometry. Taste acuity was measured by a device developed by the Otolaryngology Branch of the USAF School of Aerospace Medicine. This apparatus is based on the principle that taste receptors can be activated by small electric voltages passed across the tongue. The threshold of voltage stimulation of the taste receptors bears a close relationship to the sensitivity of the receptors, and any damage to them greatly increases the voltage threshold. The instrument, itself, consists of two small conducting paddles which are placed on either side of the tongue. A gradually increasing voltage is passed across the tongue until the subject notes a strong metallic taste.

This voltage value was taken as threshold. Threshold values ranged from 100 to 500 mv. Changes in threshold were denoted by  $(v_i - v_f)$ , where  $v_i$  was the initial voltage value and  $v_f$  was the value at the conclusion of a study.

4. Olfactometry. Olfactory acuity was also measured by a device developed by the USAF School of Aerospace Medicine, Otolaryngology Branch. Four varieties of odor--cinnamon, mint, clove, and cologne--were serially diluted by a factor of 2X in bottles numbered from 1 to 10, the former being the strongest and the latter the weakest odor. Subjects were asked to begin with the weakest bottle (No. 10) and to sniff bottles of increasing concentration until they could clearly identify the odor. Any change in olfactory threshold in this test given immediately before, and then immediately following, an experiment was noted for each of the four odors. These differences were then summed:

$$\text{Olfactory index} = \sum_{n=1}^4 (S_i - S_f) \quad (10)$$

where:

$S_i$  is the initial odor threshold;

$S_f$  is the final odor threshold; and

$1 \rightarrow 4$  are the four odors tested.

Decreases in olfactory sensitivity, therefore, led to a positive value for the olfactory index, while increases in sensitivity led to a negative index value.

### Data handling and statistical treatment

For all of the 24-hour and 48-hour experiments, data from the experimental subjects were averaged, with equal weight being given to each subject (table XIII). Since the rates of insensible water loss, both skin and respiratory, were determined in grams per square meter per hour, major differences in subject size were, for the most part, adequately compensated for. In the 10-hour experiments where two different sets of 3 subjects were utilized alternately, the mean  $IWL_S$  and  $IWL_R$  values for both sets were similar ( $\pm 2\%$ ), making it possible to compare the data sets directly.

In the wind-velocity experiments, however, subjects H.D. and L.B. were used in one set of measurements and subjects P.K. and W.C. in the second. Considering individual variation this could have resulted in considerable skewing of the data (table XIV).

In an attempt to adjust these two sets of  $IWL_S$  data so that they might be comparable with each other and with data derived from the other experiments, corrections for individual subject bias were carried out. These correction values were derived by comparing the  $IWL_S$  rate of each subject, averaged for all experiments, with the grand mean  $IWL_S$  rate for all 6 subjects in all experiments. The resulting bias values are shown in table XV. When subjects A and B formed a set, this set deviated from the grand mean by only -2.8%. When subjects D and E formed a set, the deviation from the mean was over +9.9%. The  $IWL_S$  data were corrected by utilizing a factor of 1.03 for the former set

and a factor of 0.90 for the second set. No bias corrections for  $IWL_R$  data were needed since deviations from the grand mean value were not significant.

The effects of each environmental parameter upon rates of  $IWL_S$  were initially analyzed by a comparison of differences in paired-sample means. Mean values of  $IWL_S$  for each of the subjects were tabulated for a series of experiments in which all environmental parameters except the one being examined were identical. P values were derived by looking at the T-scores of the average paired-sample differences. These values are shown on the figures relating  $IWL_S$  to the environmental parameters.

The influence of environmental conditions upon overall fluid balance and the components of total intake and output were analyzed in a similar manner. A comparison of differences of paired-sample means was utilized to derive the P values reported in the water balance figures.

A stepwise multiple regression analysis was also carried out to relate all environmental factors to rates of skin insensible water loss (10). In this analysis, 549 separate determinations of  $W_{e1}$  and 20 environmental variables were used to develop a correlation matrix. Multiple correlation coefficients, F values, T values (and corresponding P values) were derived for the significant environmental factors (table XIV).

## V. RESULTS

Results will be presented in three sections. The first will involve the relationship of skin insensible water loss ( $IWL_S$ ) as measured by  $W_{e1}$  to environmental parameters and to other experimental variables such as skin temperature and effective wall temperature. The second will involve the determinations of fluid balance and the various components of fluid loss under changing environmental conditions. In this section data on insensible respiratory water loss ( $IWL_R$ ), metabolic insensible weight loss ( $IWL_G$ ), and total insensible water loss ( $IWL_T$ ) will be tabulated. The third section will contain data on specific sign and symptom development in varying environments and the results of sensory testing in these environments.

### Skin insensible water loss ( $IWL_S$ )

Results of the direct measurement of  $IWL_S$  by the whole-body gravimetric technic are shown in table VI and figures 5 through 12. In all figures "skin insensible water loss" is synonymous with "skin insensible weight loss" since it is, in fact, an actual weight loss that is being determined. Both of these expressions can be denoted by  $IWL_S$ .

All of the environmental variables investigated: water vapor pressure ( $P_{H_2O}$ ), total barometric pressure ( $P_B$ ), ambient temperature ( $T_a$ ), wind speed ( $V$ ), and gas composition (GC)--were found to influence the rates of  $IWL_S$  to a very significant degree.



The specific effects of  $P_B$  and  $P_{H_2O}$  are seen in figure 5, where rates of skin insensible weight loss are plotted for three total pressures and a variety of water vapor pressures. At all total pressures, the  $IWL_S$  is an inverse function of the water vapor pressure at a constant  $T_a$  and  $V$ . Altering the total pressure does not change the slope of this relationship but shifts the y-intercept. The  $IWL_S$  appears to be an inverse function of total barometric pressure, as well. Thus, decreasing the  $P_{H_2O}$  from 14 mm. to 4 mm. Hg results in an increase in the rate of  $IWL_S$  of over 2.5 gm./m.<sup>2</sup>/hr. At a  $P_B$  of 480 mm. Hg (intermediate between 700 and 258 mm.), the increase in rate is almost 1.2 gm./m.<sup>2</sup>/hr., or half the above increase. A single experiment performed at 565 mm. Hg  $P_B$  demonstrates a slight increase in  $IWL_S$  rates commensurate with the relatively small increment of pressure change that was instituted. The P values for the three major barometric pressures tested indicate the statistical significance of these data.

Figure 6 again shows the relationship of  $IWL_S$  to  $P_{H_2O}$  and  $P_B$ . Here, however, the means and standard deviations of the data points are plotted. In figure 7, these same data are again shown, but with the individual data points of the 6 subjects and the total ranges of each experiment. Some subjects, such as subject D, maintained above average rates of water loss while others, such as subject F, consistently maintained lower than average rates. This pattern was consistent throughout the project.

The effects of varying atmospheric gas compositions, were studied only at 258 mm. Hg  $P_B$  (fig. 8). Most studies were run in an atmosphere of 70%  $O_2$  and 30%  $N_2$ , which at this pressure provided 180 mm. Hg of  $O_2$ . Experiments were then conducted using 100%  $O_2$  and using an oxygen-helium mixture of 70%  $O_2$ , 30% He. Although only two levels of  $P_{H_2O}$  were investigated with these gas mixtures, some general conclusions may be drawn. The rates of  $IWL_S$  in 100%  $O_2$  were higher, but not significantly so, than in the  $O_2:N_2$  atmosphere. The rates of  $IWL_S$  in the oxygen-helium atmosphere were, however, considerably lower than in either the  $O_2:N_2$  or 100%  $O_2$  atmospheres. At both the 6.5- and 9-mm. Hg  $P_{H_2O}$  measurements,  $IWL_S$  rates in the  $O_2:He$  environments were more than 20% lower. Not enough points were measured, however, to assure absolute statistical significance.

The effect of ambient temperature on rates of  $IWL_S$  is related to the  $P_B$  at which measurements are made (fig. 9). At 258 mm. Hg  $P_B$ , the effect of  $T_a$  was directly related through the range from 20° to 28° C. During this 8-degree rise in  $T_a$ , rates of  $IWL_T$  increased by more than 3 gm./m.<sup>2</sup>/hr., or 33%. This direct relationship was noted at all levels of  $P_{H_2O}$  studied (4 mm., 8 mm., and 14 mm. Hg). At a  $P_B$  of 700 mm. Hg, however, the effect of  $T_a$  was still positive but not as directly proportioned. The rate of increase of  $IWL_S$  between 24° and 28° C. was much greater than that between 20° and 24° C.  $T_a$ . This pattern appeared to hold at all levels of  $P_{H_2O}$  studied. P values indicate that the effect of  $T_a$  on  $IWL_S$  rates was highly significant.

In figure 10 the mean values and S.D. of data from two diverse environmental situations can be seen.

The interaction of  $P_{H_2O}$  with  $P_B$  and  $T_a$  in determining the rates of IWL<sub>S</sub> is shown in figure 11. For any given level of  $P_{H_2O}$ , a rise in  $T_a$  or a fall in  $P_B$  will significantly raise the rate of IWL<sub>S</sub>. The effects of temperature and total pressure appear to be uniform over the entire range of  $P_{H_2O}$  studied, as the  $P_B$ - $T_a$  lines are nearly parallel. An exception is seen in the 700 mm. Hg  $P_B$  - 28° C.  $T_a$  line. In this situation the rate of IWL<sub>S</sub> at 14 mm. Hg  $P_{H_2O}$  was much higher than would be predicted--leading to a decrease in the line slope. The high value at 14 mm. Hg  $P_B$  can be accounted for by the onset of observable thermal sweating in this high temperature-high humidity situation. This was the only experiment in the entire series where thermal sweating was detected.

The effect of wind speed (V) on the rate of skin insensible weight loss tended to be directly related over the range studied (fig. 12). A striking effect of elevated wind speeds, however, was their tendency to obliterate or cancel the effects of  $P_B$  and  $P_{H_2O}$ . At wind speeds in the 20 to 40 ft./min. (or 7 to 9 m./min.) range, the effects of varying total pressure and water vapor pressure are apparent. As demonstrated above and shown in figure 12, in the region of low wind speed or free convective cooling, lowering  $P_B$  or  $P_{H_2O}$  leads to significant changes in IWL<sub>S</sub>. As the wind speed reaches the region of forced convective cooling (in the range of 100 ft./min., or 30 m./min.), the rate of IWL<sub>S</sub>

continues to increase almost linearly. However, the absolute differences in IWL<sub>S</sub> rate related to differences in P<sub>B</sub> and P<sub>H<sub>2</sub>O</sub> continue to diminish as the wind speed rises. Above 200 ft./min. these differences are no longer significant. Whereas at 40 ft./min. V, the difference in rate of IWL<sub>S</sub> at 258 mm. Hg P<sub>B</sub> (as opposed to 700 mm. Hg P<sub>B</sub>) averaged 1.6 gm./m.<sup>2</sup>/hr., at 300 ft./min. V, this difference was only 0.6 gm./m.<sup>2</sup>/hr. At 40 ft./min. the rate difference between the two values of P<sub>H<sub>2</sub>O</sub> (9 mm. and 6.5 mm. Hg) averaged 0.8 gm./m.<sup>2</sup>/hr., while at 300 ft./min. V, this difference is only 0.1 gm./m.<sup>2</sup>/hr. Nevertheless, increasing the wind speed from 40 to 300 ft./min. led to an average increase in the rate of IWL<sub>S</sub> of 3.4 gm./m.<sup>2</sup>/hr., or 32%.

The individual effects of all environmental variables studied are summarized in table XIII and in figure 13. Here, the change in rate of IWL<sub>S</sub> produced by each variable is expressed in terms of grams per square meter per hour per Δ unit environmental change. In the case of T<sub>a</sub>, the unit of environmental change is 1° C.; for P<sub>H<sub>2</sub>O</sub>, it is 1 mm. Hg; for P<sub>B</sub>, it is 100 mm. Hg; and for V, it is 50 ft./min. Whereas increases in T<sub>a</sub> and V cause increases in the rate of IWL<sub>S</sub>, increases in P<sub>B</sub> and P<sub>H<sub>2</sub>O</sub> cause decreases in the rate of IWL<sub>S</sub>. Although most of the environmental variables show almost linear effects over the ranges studied, T<sub>a</sub> demonstrates a varying effect in its high and low ranges.

The possible role of average skin temperature as a determinant of the rates of skin IWL was also investigated. It became apparent in experiments run at different total pressures, but otherwise

identical ambient conditions, that skin temperatures always were higher at lower barometric pressures. For a given  $T_a$ , skin temperatures were as much as  $0.8^\circ \text{C}$ . higher at 258 mm. Hg  $P_B$  than at 700 mm. Hg  $P_B$  (figure 14). This skin temperature difference was noted only with low wind speed and was abolished by  $V$  higher than 100 ft./min.

In figure 15 a large number of  $IWL_S$  rates measured at varying environmental conditions are plotted against skin temperature. Several features are apparent. Most prominent--although a wide scatter is present--is the apparent direct correlation between skin temperature and rates of  $IWL_S$ . Because of the wide scatter, however, it is unlikely that skin temperature is the only variable involved in the determination of  $IWL_S$  rates. A second important feature is the profound effect of elevated wind velocities in increasing the rates of  $IWL_S$  for a given skin temperature. At  $V$  greater than 100 ft./min., higher rates of  $IWL_S$  were noted at lower skin temperatures than were encountered in quieter air. A final feature to be noted is the lack of clear differentiation between the data points of 258 mm. Hg and those of 700 mm. Hg  $P_B$ . This feature would suggest that the effect of  $P_B$  on rates of  $IWL_S$  is partially mediated by changes in skin temperature.

Another possible determinant of skin insensible water loss rates that was investigated was effective wall temperature ( $T_{ew}$ ). As discussed above,  $T_{ew}$  was thought to reflect the total effective radiative heat load on the subjects while they were lying on the metabolic scale.

This parameter was consistently higher than ambient temperature (table VI), with the most striking elevations noted with reduced  $P_B$  and with elevated V. In the stepwise multiple regression analysis (table XIV),  $T_{ew}$  was found to have the greatest correlation with  $IWL_S$  of any single environmental measurement. A correlation coefficient of .530 and a P value of less than .001 were noted.

In addition to  $T_{ew}$ , high correlations were noted with  $P_{H_2O}$ ,  $T_a$ , V, and  $P_B$ . The average molecular weight of the atmospheric gases also exhibited a surprisingly high correlation with  $IWL_S$ , having a P of .001. When a multiple correlation coefficient including all six of the important environmental measurements was derived, a value of .684 resulted.

In all of the experiments in which rates of  $IWL_S$  were measured, a mean value expressed in grams per square meter per hour was derived from the individual subject values. As noted above, some subjects consistently ran close to the average, while others ran above or below the average with the same consistency. In table XV the overall deviations from the grand mean  $IWL_S$  value in a large number of experiments are shown for each of the 7 experimental subjects. Five of the subjects deviated less than  $\pm 6\%$  from the grand mean in their own mean values, while the remaining 2 deviated by close to  $\pm 15\%$ . In all experiments, subject P.K. tended to produce the highest value in the range, while subject M.K. produced the lowest value.

Intra-subject variations--i.e., variations from measurement to measurement in a single subject--in  $IWL_g$  rates occurred in all experiments. In the 48-hour studies where four separate determinations of skin water loss were made, differences of up to  $2 \text{ gm./m.}^2/\text{hr.}$  were observed in a single subject under fixed environmental conditions. An analysis of replicate runs, however, failed to show any significant time trends or any relationship to time spent in the environmental chamber.

The means, standard deviations, and standard errors for the four sets of replicate runs by the 6 subjects are shown in table XVI for two typical experiments. In these 12 sets of replicate runs (4 runs per set), the S.D. ranged from .32 to 1.52, and the S.E. from .16 to .75. All values are expressed in grams per square meter per hour.

#### Fluid balance studies

Complete intake and output studies were done on all subjects in experiments lasting 24 hours or longer (27 experiments). Data collected or computed included total intake ( $W_I$ ), total output ( $W_O$ ), change in body weight ( $\Delta W$ ), total respiratory water loss ( $W_{R_t}$ ), total direct skin insensible weight loss ( $W_{e_{1_t}}$ ), total indirect skin insensible weight loss ( $W_{e_{2_t}}$ ), grand total output ( $W_O + W_{e_{1_t}}$ ), and total insensible weight loss ( $IWL_T$ ). Mean values for each of the 27 experiments are shown in table VI, along with partial data from the 11 shorter studies.

To ascertain whether fluid balance was maintained in a relatively steady state at the start of the project, total intake and grand total output were compared during the initial 7 experiments which occupied the first 20 project days (fig. 16). During these experiments, total intake was relatively constant averaging 2,380 gm., while grand total output averaged 2,070 gm. No 24-hour intake varied more than 120 gm. from the mean, and no 24-hour output more than 150 gm. The discrepancy between total intake and grand total output was expected and will be discussed.

That the experimental subjects maintained a relatively constant overall weight balance throughout the 12-week study can be seen in table VIII. In 4 of the 7 subjects, the maximum weight change (initial minus final) during the entire experiment was less than 450 gm. In a fifth, the change barely exceeded 1,000 gm. In subject E, however, a steady increase in weight occurred, resulting in a net weight gain of 3,116 gm. during the experimental period. No ready explanation for this unusual gain could be offered except that this subject was consistently receiving a larger caloric intake than his overall activity level could utilize.

The individual effects of 4 of the 5 environmental parameters discussed above upon the maintenance of fluid balance were investigated. The effect of  $P_B$  upon fluid balance and the routes of insensible water loss was determined by pairing all experiments which were alike in physical parameters other than  $P_B$  (fig. 17). Total intake in the



258 mm. Hg  $P_B$  experiments averaged 140 gm./24 hr. more than in the 700 mm. Hg experiments. This difference was significant to the .05 level. The difference in grand total output was even more striking and in the opposite direction, with the 258 mm. Hg  $P_B$  experiments averaging 260 gm. less than the 700 mm. Hg. This was significant to the .01 level. Differences in respiratory water loss, skin insensible water loss, and total insensible water loss at the two levels of  $P_B$  were also significant at the .05, the .01, and the .1 levels, respectively. No significant differences in weight change could be detected, although subjects tended to lose weight at 700 mm. Hg  $P_B$  and gain weight at 258 mm. Hg  $P_B$ .

The effect of changes in  $P_{H_2O}$  on fluid balance is seen in figure 18. Here, differences in  $W_I$  at the three values of  $P_{H_2O}$  are not statistically significant, while differences in grand total output are significant to the .05 level.  $W_R$  increases significantly ( $P < .01$ ) with decreasing  $P_{H_2O}$ , while  $W_{e_{1t}}$  and  $IWL_T$  also increase significantly ( $P < .01$ ). Weight changes are again not significant.

Changes in  $T_a$  also affect fluid balance (fig. 19). With higher ambient temperatures, there is a significant increase in  $W_I$ , coupled with a barely significant decrease in  $W_O$ . At 28° C.  $W_I$  averaged 260 gm. higher than at 20° C., while  $W_O$  averaged 210 gm. lower. Significant increases in  $W_R$ ,  $W_{e_{1t}}$ , and  $IWL_T$ , with increasing ambient temperature, were also noted. Again, weight changes were not statistically significant, although a tendency to gain weight at higher temperatures was noted.

Finally, the effect of varying gas composition at 258 mm. Hg  $P_B$  was examined (fig. 20). In paired experiments it was noted that the only statistically significant weight differences in the three atmospheres involved  $W_{e1t}$  ( $P < .05$ ) and  $IWL_T$  ( $P < .05$ ), when  $N_2$  was replaced by He.

By use of the total weight balance equations discussed above, an indirect calculation of skin insensible weight loss was accomplished ( $W_{e2t}$ ) in the 27 experiments, where complete intake and output measurements were done. The values of  $W_{e2t}$  are given in table VI, together with a comparison of values of  $W_{e1t}$  and the difference between these two values for skin IWL. In almost all cases the value of  $W_{e2t}$  is higher than that of  $W_{e1t}$ . In 27 of 28 experiments, however, this difference is less than 400 gm./24 hr., and in 21 of 28 experiments it is less than 250 gm./24 hr.

Direct and indirect calculations of  $IWL_S/24$  hr. at varying  $P_{H_2O}$  and  $T_a$  are shown in figures 21 and 22. It is again apparent that the indirect calculation ( $W_{e2t}$ ) produces a higher loss value than the direct measurement ( $W_{e1t}$ ). At higher wind speeds, values for  $W_{e1t}$  are greater than at low speeds, but the effects of  $P_B$  and  $P_{H_2O}$  are again muted.

Insensible respiratory loss rates ( $W_R$ ) for all experiments are given in table VI and are expressed as both grams per square meter per hour and total grams. The relationship of  $W_R$  to  $P_{H_2O}$  is seen in figure 23, where values for 700 mm. Hg  $P_B$  and 258 mm. Hg  $P_B$  are

plotted separately. Rates of insensible respiratory water loss increase rapidly and nonlinearly with a decrease in  $P_{H_2O}$ . At a reduced  $P_B$  this increase is less rapid; at 258 mm. Hg  $P_B$ ,  $W_R$  increases by only 3.0 gm./m.<sup>2</sup>/hr. from 14 to 4 mm. Hg  $P_{H_2O}$ , while at 700 mm. Hg  $P_B$ ,  $W_R$  increases 3.9 gm./m.<sup>2</sup>/hr. over the same range of  $P_{H_2O}$ . At 14 mm. Hg  $P_{H_2O}$  the difference in  $W_R$ , comparing 700 mm. Hg  $P_B$  with 258 mm. Hg  $P_B$ , is only 9%; while at 4 mm. Hg  $P_{H_2O}$  this difference has increased slightly to 13%.

Rates of  $IWL_R$  also increase rapidly and nonlinearly with increases in  $T_a$  (fig. 24). At 258 mm. Hg  $P_B$  this increase is less rapid than at 700 mm. Hg. Increasing the ambient temperature from 20° to 28° C. results in an increase in  $W_R$  of 2.3 gm./m.<sup>2</sup>/hr. at 258 mm. Hg  $P_B$ , and an increase of 2.9 gm./m.<sup>2</sup>/hr. at 700 mm. Hg. At 20° C.  $T_a$  the difference in  $W_R$  comparing 700 mm. Hg  $P_B$  with 258 mm. Hg  $P_B$  is 8%, while at 28° C. this difference is 11%.

If the rates of  $W_R$  are plotted only against the relative humidity (R.H.) of the inspired air, an interesting relationship can be seen regardless of  $T_a$  or  $P_{H_2O}$  (fig. 25);  $W_R$  appears to be related only to R.H. and to  $P_B$ , with all data points falling on the two  $P_B$  lines despite variations in ambient temperature. Again the relationship to R.H. is nonlinear, with a more rapid increase in  $W_R$  at the higher total pressure (700 mm. Hg) than at the lower (258 mm. Hg). The average pulmonary ventilation rates in liters per hour are shown, and the ventilation at 258 mm. Hg  $P_B$  is 10% lower than

at 700 mm. Hg. This 10% difference in ventilation rates could account for almost all of the observed differences in  $W_R$  at the two total pressures.

If the rates of skin insensible water loss ( $W_{e1}$ ) are plotted in a similar manner against R.H. (fig. 26), a relationship to R.H. and  $P_B$  also exists, but the values are also strongly influenced by changes in ambient temperature. This indicates an effect of  $T_a$  upon  $IWL_S$  which is independent of the effect of  $T_a$  upon ambient relative humidity.

Total insensible weight loss measurements ( $IWL_T$ ) were computed for all 38 experiments in both grams per square meter per hour and in grams per 24 hour (table VI). Values ranged from lows of 10.4 gm./m.<sup>2</sup>/hr. and 496.8 gm./24 hr. to highs of 22.6 gm./m.<sup>2</sup>/hr. and 1,065.2 gm./24 hr. In all  $P_{H_2O}$  conditions values of  $IWL_T$  were greater at 258 mm. Hg  $P_B$  than at 700 mm. Hg  $P_B$  (fig. 27). This difference tended to diminish, however, as  $P_{H_2O}$  decreased, largely because of the increasing contribution of  $IWL_R$  at the lower water vapor levels. At 4 mm. Hg  $P_{H_2O}$ , in fact,  $IWL_R$  actually exceeded  $IWL_S$  at 700 mm. Hg  $P_B$ . In all other cases,  $IWL_S$  was substantially larger than  $IWL_R$ , and the contribution of  $IWL_G$  was minor and relatively constant.

The effect of  $T_a$  on the components of  $IWL_T$  is seen in figure 28. At 20° and 24° C.  $T_a$ ,  $IWL_T$  is considerably greater for 258 mm. Hg  $P_B$  than for 700 mm. Hg  $P_B$ . At 28°  $T_a$ , however,  $IWL_T$  is actually slightly greater for 700 mm. Hg  $P_B$  than for 258 mm. Hg  $P_B$ . This reversal is

caused by the increasing difference in  $IWL_R$  with rising temperature at the two pressures, coupled with an increased rate of  $IWL_S$  with rising temperature at 700 mm. Hg.  $IWL_G$  diminishes very slightly as  $T_a$  rises. As expected, maximum values for  $IWL_T$  are seen at 28° C. and minimum values at 20° C.  $T_a$  regardless of total pressure.

Surveying all 38 experiments, it can be seen that the contribution of  $IWL_S$ ,  $IWL_R$ , and  $IWL_G$  to total insensible weight loss ( $IWL_T$ ) shows considerable variation (examples are shown in fig. 29). In a low  $P_B$ , high  $P_{H_2O}$ , and low  $T_a$  experiment, skin insensible weight loss comprised 60.9% of the  $IWL_T$ , with respiratory insensible loss contributing only 25.5% and  $IWL_G$  13.6%. In a high  $P_B$ , low  $P_{H_2O}$ , intermediate  $T_a$  experiment,  $IWL_S$  comprised only 48.5% of  $IWL_T$ , while  $IWL_R$  contributed an almost equal 43.9%.  $IWL_G$  contributed only 7.6% of the total. In an intermediate environmental situation,  $IWL_S$  contributed 53.4%,  $IWL_R$  39.3%, and  $IWL_G$  7.3% to the  $IWL_T$ .

#### Sign and symptom development

Sign and symptom frequency-severity index values for experiments lasting 24 hours or longer are summarized in table XVII. In all cases the Symptom Index (subjective evaluation by subjects) was the more sensitive indicator of a response to the environment. The mean Symptom Index value for all experiments was  $-.79$ , as compared to a  $-.44$  for the Subject Sign Index and a  $-.24$  for the Physician Sign Index. Both Sign- and Symptom-Index values became more negative as  $P_{H_2O}$  diminished, with the Sign-Symptom Index falling from  $-0.36$  to  $-0.74$  when  $P_{H_2O}$  was varied from 14 mm. to 4.5 mm. Hg.

Sign and symptom development as related to  $P_B$  and  $P_{H_2O}$  in all experiments of 24 hours or longer duration is shown in figure 30. "Symptoms Only" values are derived from the Symptom Index, while "Signs and Symptoms" values are derived from the Sign-Symptom Index. Both signs and symptoms were more severe at 258 mm. Hg  $P_B$  than at 700 mm. Hg  $P_B$  at almost all levels of  $P_{H_2O}$ . At 700 mm. Hg  $P_B$  a sharp increase in both signs and symptoms began only after  $P_{H_2O}$  had been reduced below 6.5 mm. Hg. At 258 mm. Hg  $P_B$ , on the other hand, a sharp increase in signs and symptoms began when  $P_{H_2O}$  had fallen below 9 mm. Hg. At 4 mm. Hg  $P_B$ , signs and symptoms increased rapidly regardless of total pressure.

When only the 48-hour experiments are examined, similar results can be seen (fig. 31). Whereas the symptom index remains relatively constant as  $P_{H_2O}$  is reduced from 14 mm. Hg to 6.5 mm. Hg at a  $P_B$  of 700 mm. Hg, a steep rise in the index occurs at 9 mm. Hg  $P_{H_2O}$  when  $P_B$  is reduced to 258 mm. Hg.

The effect of ambient temperature upon the development of signs and symptoms is also significant (fig. 32). Between 24° and 28° C. there is relatively little change in signs or symptoms. As the  $T_a$  falls to 20° C., however, a dramatic increase in symptom severity occurs with 700 mm. Hg  $P_B$ ; this increase is not seen with 258 mm. Hg  $P_B$ . A similar but less important change also occurs in the sign-symptom index. Subjects appeared to be more adversely affected by the colder  $T_a$  at normal pressures (700 mm. Hg) than at lower total pressures (258 mm. Hg).

The timecourse of symptom and sign development was examined only in the 48-hour experiments. Symptom development over a 48-hour period at four levels of  $P_{H_2O}$  and two levels of  $P_B$  are shown in figures 33 and 34, respectively. At 14 mm. Hg  $P_{H_2O}$  a very gradual and slight decrease in the symptom index occurred during the first 18 hours, leveling off thereafter. A minimum value of -0.6 was noted at 258 mm. Hg, and a value of -0.54 at 700 mm. Hg  $P_B$ .

At 4 to 5 mm. Hg  $P_{H_2O}$  changes were more rapid and severe. During the first 18 to 20 hours, index values rose steeply with the sharpest changes in the first 6 hours. After the first 20 hours, index values remained relatively constant with a minimal value of -1.2 attained at 700 mm. Hg, and a value of -1.3 reached at 258 mm. Hg  $P_B$ .

As expected the time course of symptom changes at 6.5 mm. and 9 mm. Hg  $P_{H_2O}$  fell between that for 4.5 mm. and 14 mm. Hg  $P_{H_2O}$ . An increase in symptoms was again noted over the first 20 hours followed by a leveling off. At any point in time, symptoms were usually more severe at 258 mm. Hg than at 700 mm. Hg  $P_B$ . At 9 mm. Hg  $P_{H_2O}$ , the effect of  $P_B$  on the rate and severity of symptom development was particularly evident, with a 32% index difference between 700 mm. and 258 mm. Hg after 12 hours.

Sign development over a 48-hour period at four levels of  $P_{H_2O}$  and two levels of  $P_B$  is shown in figures 35 and 36, respectively.

Changes here paralleled those noted in symptom development. At 14 mm. Hg  $P_{H_2O}$  a slight change in sign severity occurred over the first 10 hours. At 4 to 5 mm. Hg  $P_{H_2O}$  a rapid change in the index took place during the first 18 hours with the steepest change in the first 6 hours. A minimum value of -1.0 was reached for 700 mm. Hg, and a value of -1.1 for 258 mm. Hg  $P_B$ . After the first 20 hours few changes were noted.

With a  $P_{H_2O}$  of 9 mm. Hg a striking difference in sign development related to  $P_B$  was seen. In the 258 mm. Hg experiment, a low index value was present from the very start and changed only slightly through the entire run. This initial low value was produced by the fact that 2 of the experimental subjects had developed viral sore throats before the start of the experiment and presented signs of throat irritation well out of proportion to their symptoms. Very little progression of these signs was noted during the 48 hours of the experiment; however. At all levels of  $P_{H_2O}$ , sign development was generally more rapid and more severe at 258 mm. Hg  $P_B$  than at 700 mm. Hg.

The effects of  $P_B$ ,  $P_{H_2O}$ ,  $T_a$ , and GC on the frequency and severity of sign and symptom development in each of the anatomical areas or categories evaluated for the indices are shown in figures 37 through 46. In a summary of all experiments, 24 hours or longer (fig. 37), the "Nose" category was the most frequently and severely involved in respect to symptoms. In decreasing order, there followed "Lips," "Pharynx," "Eyes," "Mouth," "Tongue," "Scalp," "Skin," and



General." Nose symptoms were reported with 62% greater frequency or severity than lip symptoms and with 970% greater frequency or severity than general symptoms.

The effect of barometric pressure ( $P_B$ ) on area-specific symptoms is seen in figure 38. Except for the pharynx, tongue, and skin, symptoms were more severe in each area at 258 mm. Hg than at 700 mm. Hg  $P_B$ . Looking at the mean value, symptoms at 258 mm. Hg averaged 23% greater in frequency-severity than at 700 mm. Hg. The effect of  $P_{H_2O}$  on area-specific symptoms (fig. 39) is similar. Except for the pharynx, symptoms were substantially more frequent or severe at the lower value of  $P_{H_2O}$  than at the higher. In terms of the mean value, symptoms were 85% greater at 4 mm. Hg than at 14 mm. Hg  $P_{H_2O}$ .

When the effect of  $T_a$  upon the severity and frequency of symptom development by anatomical region was examined (fig. 40), an unusual pattern emerged. A striking effect of  $T_a$  upon nose symptoms was seen, with a greater than 100% increase noted between 28° and 20° C. In all other anatomical regions except the general category, however, this temperature effect was minimal, if visible at all. With lips and pharynx, in fact, the temperature effect was reversed, with greater symptoms occurring at the higher  $T_a$ . At 20° C.  $T_a$  subjects very frequently complained of increased nasal stuffiness and coryza along with some general discomfort, while other symptoms were not apparent.

The influence of gas composition at 258 mm. Hg  $P_B$  on area-specific symptoms was not consistent (fig. 41). Although an increase in symptom severity did occur in 100%  $O_2$  in 6 of the 9 categories, not all of the differences could be called significant. In the  $O_2:He$  atmosphere, a decrease in symptoms from the  $O_2:N_2$  mixture was also noted in 6 of the 9 categories. In terms of the mean values, symptoms were 12% more prominent at 100%  $O_2$ , and 6% less prominent in  $O_2:He$  when compared to the  $O_2:N_2$  atmosphere.

The frequency-severity of signs related to anatomical areas presented quite a different picture. In figure 42, area-specific signs in all experiments 24 hours or longer are shown. The physician evaluation and the subject evaluation are plotted separately and the physician-subject mean value (sign frequency-severity index) is shown. The order of frequency-severity for signs is clearly different from the order of symptoms. Here, the "Lips" category was most prominent followed by "Eyes," "Nose," "Tongue," "Pharynx," "Mouth," "Skin," "Scalp," and General." Whereas, the "Nose" category was most prominent among symptoms, it occupied only 3d place among signs. While "Eyes" held 4th place in symptoms, it moved up to 2d place in signs. As "Lips" moved up from 2d position in symptoms to 1st position in signs, "Pharynx" fell from 3d to 6th. In these experiments lip signs were noted with 33% greater frequency-severity than eye signs, 122% greater frequency-severity than nose signs, and 2,500% greater frequency-severity than general signs.

The effect of  $P_B$  on sign development by area was less striking than its effect on symptom development (fig. 43). A significant increase in severity of signs at 258 mm. Hg as opposed to 700 mm. Hg was noted in lips, eyes, mouth, and scalp. The mean value difference amounted to only 15%, however. In the nose and pharynx area, signs were actually less severe at the lower  $P_B$ .

Water vapor pressure produced a more consistent effect (fig. 44). Sign frequency-severity was more notable at 4 mm. Hg  $P_{H_2O}$  than at 14 mm. Hg in 8 of the 9 anatomical categories. Only the tongue area failed to show this vapor pressure effect. In the lip area the increase in signs from 14 mm. Hg to 4 mm. Hg  $P_{H_2O}$  was over 137%, and the mean value for all areas jumped 117%.

The influence of  $T_a$  was found to be minimal (fig. 45). An increase in signs in the lip and eye areas was seen with a rise in  $T_a$ , but a decrease in signs was noted in the tongue, pharynx, mouth, skin, and general areas. The mean value difference between 20° and 28° C.  $T_a$  was only 15%, with the edge going to 20° C.

The effect of gas composition at 258 mm. Hg  $P_B$  on regional sign development is shown in figure 46. In 100%  $O_2$ , the frequency-severity of signs was slightly higher in the lip, tongue, mouth, and skin areas when compared with the other gas mixtures. In 70%  $N_2$ :30% He, signs were slightly less severe in the lip, nose, tongue, and mouth areas when compared with the other atmospheres. The mean sign values, however showed only a 10% difference in frequency-severity between the 100%  $O_2$  and the  $O_2$ :He atmospheres.

A comparison of anatomical areas in terms of sign and symptom development is shown in table XVIII. The specific symptom or sign that occurred with the greatest frequency in each region is also listed.

The relationship of sign and symptom development to rates of skin insensible water loss and to total insensible water loss is shown in figure 47. A set of environmental parameters which produced a low rate of  $IWL_S$  (designated as "A") was used as a baseline for measurements in two environments which produced a high rate of  $IWL_S$  (designated as "B" and "C"). All measurements of changes in "B" and "C" are expressed as a percentage change for "A". Whereas,  $IWL_S$  increased by 117% and 108% in environments "B" and "C," respectively,  $IWL_T$  increased by 94% and 117%. The increase in the sign-symptom indices in these two environments were very similar to the increases in  $IWL_S$  and  $IWL_T$ , 130% for "B," and 140% for "C." The increase in  $IWL_R$ , on the other hand, did not accurately reflect the changes in the sign-symptom indices.

The correlation between rates of skin insensible water loss and the sign-symptom index over the entire range of this experiment is shown in figure 48. Both parameters are expressed as a percent increase over the baseline values. The relationship is curvilinear, with very little change in the sign-symptom index occurring with increases in  $IWL_S$  of up to 50% over the baseline. With still higher rates of  $IWL_S$ , however, the rate of increase in the sign-symptom index accelerates so that a 120% increase in  $IWL_S$  is associated with a 100% increase in the index.

A summary of the results of the specific sensory tests performed during the 24- and 48-hour experiments is shown in table XIX. Only those changes which have some statistical significance are listed. Visual acuity alterations were found to be minimal in almost all experiments, the exception being the two 48-hour studies run at very low levels of  $P_{H_2O}$ . During these two studies subjects reported increased eye irritation in the chambers.

Schirmer's test results were very difficult to interpret, and significant changes were noted in only three experiments with a wide variety of ambient conditions. Tearing appeared to decrease in some atmospheres featuring low  $P_{H_2O}$  or high  $T_a$ . Gustometry results indicated that some atmospheres tended to diminish taste acuity while others actually increased acuity. The most striking decrease in taste ability occurred with low  $P_B$  and low  $P_{H_2O}$ . In both experiments utilizing  $O_2:He$  atmospheres, taste ability was significantly improved. Changes in olfactory function were also difficult to document, with significant changes occurring in only two experiments. Both of these featured low  $P_{H_2O}$  and low  $P_B$ , and smell was significantly decreased.

## VI. DISCUSSION

### Skin insensible water loss:

The measurement of  $IWL_S$  by the whole-body gravimetric method has a long history in the scientific literature (20, 32, 50, 56, 62, 65, 114, 122). Other methods such as the dessicated capsule, diffusion chamber, CaCl bag, electrohygrometry-airflow, gravimetric-airflow, and infrared-airflow systems have fallen in and out of favor (table II). Each of these methods possesses inherent difficulties and errors, and all do not measure identical types of water loss from the skin.

The whole-body gravimetric technic which was selected for this study measures the average rate of weight loss from the entire body. Therefore, not only the so-called diffusional water losses are measured, but all losses - including mental sweating, thermal sweating (if present), metabolic gas exchange, and respiratory water. By utilizing special technics to trap respiratory water and to calculate metabolic gas exchange and by selecting environmental conditions under which thermal sweating will not occur, one is able to measure  $IWL_S$  alone (as  $W_e$ , which includes  $W_D$  and  $W_M$ ).

All technics which utilize a skin capsule or diffusion chamber to collect water vapor (3, 14, 17, 24, 26, 27, 41, 53, 60, 69, 73, 83, 86, 92, 103, 107, 129) - no matter how the amount of water is actually measured - can look only at rates of skin water loss

from small anatomical areas. Since these areas are usually located on the abdomen, trunk, or forearm (where mental sweating is not present), these techniques are actually measuring only  $W_D$ , or diffusional water loss. Numerous studies have shown that palmar, plantar, axillary, and head skin are responsible for more than 55% of evaporative heat loss under nonsweating conditions, while making up less than 22% of the body surface area (60, 73). It is these areas which feature significant mental sweating from secretory glands and which give evidence that  $W_M$  usually plays a significant role in skin insensible water loss. This role is neglected in the skin capsule technic in which skin areas with prominent mental sweating are not covered.

Utilization of the skin capsule or diffusion chamber technics, also brings some uncertainty as to the accuracy or applicability of the values of  $IWL_g$  which are obtained. In the measurement of evaporative rates by these technics, it is impossible to quantitate precisely the ambient conditions at the skin surface under the capsule (92). If a still-air method is used (dessicated capsule), one cannot easily maintain a fixed temperature or water vapor pressure under the capsule. In order for  $IWL_g$  values to be valid, one must assume that the skin will adjust to the new set of conditions in effect when the capsule is fixed to the skin.

When an airflow method is used, the validity of  $IWL_g$  readings

is even more suspect. Peiss and Hertzman (92) demonstrated that the collection of water vapor by a moving stream of dry air imposes severe demands upon the skin by dramatically increasing the vapor pressure difference between skin and the air which overlies it. The moving stream of air also induces turbulence at the skin-air interface, and thus creates an "unnatural" environment for water diffusion and evaporation (24). Whether IWL<sub>g</sub> rates determined under these conditions accurately reflect normal values is open to considerable question.

A recent study has also demonstrated that measurements of skin water loss rates utilizing the airflow and skin capsule technics are effected not only by the velocity and humidity of the airstream, but also by the size of the capsule and the area of skin that it covers (64). The actual rate of airflow over the skin surface will vary with the shape and size of the subcapsular space overlying the skin, as well as with the measured flow rate of gas into or out of the capsule. As pointed out by Tregear (in Johnson and Shuster, 64) one is always faced with the problem of separating the changes in IWL<sub>g</sub> which are related to the skin from those which are related to differences in air movement. In all of these studies the technics used to measure skin water loss significantly change the environment in which the water loss is to be measured.

The examination of previous experimental determinations of skin IWL rates (table II) reveals that values determined by the whole-body gravimetric technic (20, 50, 56, 62, 65, 114, 122) and by the



dessicated skin capsule technic (24, 26, 60, 69, 92) are in close agreement, with a mean value for the former set of  $10.97 \text{ gm./m.}^2/\text{hr.}$ , and for the latter set of  $10.69 \text{ gm./m.}^2/\text{hr.}$  It should be noted that those values determined by the dessicated capsule method often represent averages from multiple anatomical sites including palms and soles.

Measurements using other technics show wide variations, with the electrohygrometry-airflow studies giving a range from 1.5 to  $17 \text{ gm./m.}^2/\text{hr.}$  and the gravimetric-airflow studies, a range from 2.5 to  $58.0 \text{ gm./m.}^2/\text{hr.}$

Rates of  $IWL_S$  in this study ranged from 6 to  $15 \text{ gm./m.}^2/\text{hr.}$ , with an average value of  $9.57 \text{ gm./m.}^2/\text{hr.}$  at  $760 \text{ mm. Hg } P_B$  and  $24^\circ$  to  $28^\circ \text{ C. } T_a$ . These rates compare very closely with those determined by other investigators who have used the whole-body gravimetric or the dessicated capsule technics.

Using electrohygrometry and dry airflow, several investigators have recently shown consistent results in measuring "transepidermal water loss" from the flexor aspect of the forearm (43, 64, 105). Values of 1.8 to  $3.5 \text{ gm./m.}^2/\text{hr.}$  were obtained when experimental technics and anatomical sites were standardized. These measured rates of transepidermal water loss represent a skin area which shows little or no evidence of mental sweating or sweat gland activity below the thermal threshold. It is also an area in which skin resistance to water diffusion is notably high. (92).

It is, therefore, apparent that this skin water loss represents only  $W_D$ , or diffusional water, and that this measurement of  $W_D$  is not

representative of the entire skin surface. These factors again make it impossible to draw any conclusions about total-body water losses.

Because of the wide variation in experimental determinations of IWL<sub>g</sub>, and because of the questionable effects of environmental conditions, physiologic state of the subject, and technics of measurement, the mechanism of skin insensible water loss is still disputed. The most widely accepted concept - as amplified by Buettner (21, 22, 24) and supported by McCutchan and Taylor (78, 79), Hale et al. (56) Burch and Winsor (26), and others - holds that most skin water loss results from the continuous passive diffusion of water through the epidermis. This water loss takes place through a passive process, and the rate of loss is determined only by the physical characteristics of the epidermis and the environmental conditions of the surrounding air. A simplified equation to describe the water loss is:

$$\text{Water transfer rate per unit area} = -k (VP_s - VP_a) \quad (11)$$

where  $VP_s$  is the  $P_{H_2O}$  at skin temperature,  $VP_a$  is the  $P_{H_2O}$  at ambient temperature, and  $K$  is the permeability constant (6).

In this diffusional water loss ( $W_D$ ) approach, the skin appendages - i.e., eccrine, apocrine, or holocrine glands - are classically thought to play no role. Support for this concept is derived from experiments on subjects in whom sweat glands are congenitally absent (72, 100, 109) or have been chemically inactivated (14, 27, 95, 119). These subjects all show local rates of skin water loss generally comparable to those of normal subjects - a fact which led Pinson (95) to conclude that

"no part of the insensible perspiration of normal skin is secreted by sweat glands." The holocrine or sebaceous glands have also been eliminated as a contributor to  $W_D$  by the small volume of their secretions and the low water content (84).

If a large part of skin insensible perspiration arises by a simple diffusion process, then rates of  $IWL_S$  should be largely dependent only upon the vapor pressure gradient between skin and ambient air. Many studies (24, 28, 114) have indeed concluded that this vapor pressure gradient is an important determinant of  $IWL_S$  rates, but it has become apparent that other environmental factors such as temperature, air movement, and total barometric pressure also influence the rate of skin water loss.

Taylor and Buettner (113) have restated the effect of the environment upon  $IWL_S$  in an "evaporative effect principle": environmental properties which facilitate the evaporation of water from the skin also increase the rate of skin water loss independently of skin temperature or humidity. When evaporative forces are low, as in a high-humidity, low-temperature, high-barometric pressure, and low wind-velocity environment, diffusion of water vapor out of the skin is inhibited by an increase in skin wetness and a repenetration of surface water (96, 97; 111). Support for the evaporative effect has come from the work of Pinson (95), Taylor and Marbarger (112), Hale et al. (56) and McCutchan and Taylor (76, 79). Gagge (44) introduced the equation:

$$E = k_e w (p_s - p_a) \quad (12)$$

to describe the evaporative loss from a skin surface, where:

$E$  is the water loss in grams per square meter per hour;  
 $k_e$  is the vapor conductance between skin surface and atmosphere;

$w$  is the wetted proportion of the skin surface;

$p_s$  is the vapor pressure of the skin; and

$p_a$  is the vapor pressure of the atmosphere.

The vapor conductance term ( $k_e$ ) is dependent upon air movement and total barometric pressure as well as upon the atmospheric gas composition.

Further support for a diffusion and evaporation origin of skin insensible water loss comes from studies of the epithelial barrier to water vapor in intact and excised normal human skin. Burch and Winsor (26, 27) demonstrated that excised and clearly dead human skin retained a normal barrier to water vapor transpiration. Other experiments show that the vapor barrier properties of the stratum corneum are not dependent upon living epidermal cells, functioning enzyme systems, nor intact cell membranes (16, 73, 83, 89, 107). Several investigators (73, 89) have succeeded in localizing the water barrier to the inner two-thirds of the stratum corneum and have characterized it as a hydrophilic lipid-protein complex. Destruction of this barrier by stripping of the stratum corneum or the application of lipid solvents results in a 67-fold increase in water loss with rates of up to 300 gm./

m.<sup>2</sup>/hr. (83).

A recent study by Goodman and Wolf (50), however, has presented data to challenge the passive diffusion-evaporation concept of skin insensible water loss. Using the skin-capsule and dry airflow techniques, they measured insensible water loss from small areas of the human skin by means of infrared gas analysis. Because the relationship between ambient vapor pressure and rate of skin water loss was found to be nonlinear, these investigators proposed the alternate hypothesis that only part of  $IWL_g$  is caused by water that has passively diffused through an inert epidermal barrier. The bulk of  $IWL_g$  is due, rather, to the evaporation of water from eccrine sweat ducts, which are assumed to be filled to the top with water. They conclude that the observed influence of ambient vapor pressure on  $IWL_g$  is related not to the passive diffusional component but rather to the eccrine duct component (91).

There is little evidence in the literature to support the concept that eccrine sweat ducts are filled with water when they are inactive and thermal stimuli are not present. Indeed, there is a strong indication that the tubular epithelium of the eccrine sweat duct unit actively reabsorbs fluid (71, 115). Even at low rates of active secretion, therefore, reabsorption may exceed secretion and the ducts may not fill completely. Unless all eccrine sweat ducts are constantly filled right to the epidermal surface

with water, evaporation from these ducts is not nearly sufficient to account for bulk of skin insensible water loss (91).

All of the data presented here (figs. 5 through 13), relating skin insensible weight loss to environmental variables, are most compatible with the passive diffusion-evaporation theory of IWLs. Contrary to the findings of Goodman and Wolf (50), a nearly linear and inverse relationship was observed between ambient water vapor pressure ( $P_{H_2O}$ ) and IWLs. Such a relationship had previously been described by Taylor and Buettner (113), Hale et al. (56), Thauer et al. (114), and Kerslake et al. (65) up to a  $P_{H_2O}$  of 16 mm Hg. Over the measured range from 4 to 14 mm. Hg  $P_{H_2O}$ , the change in rate of IWLs was consistently  $-0.27 \text{ gm./m.}^2/\text{hr.}$  for every 1 mm. Hg  $P_{H_2O}$  increase.

The conflicting findings of Goodman and Wolf may be related to several differences in experimental methods. The use of a skin capsule technic provides data only from small, localized skin areas which may or may not have mental eccrine activity. The use of an airflow system of water collection alters the ambient conditions at the skin-air interface, leading to changes in diffusion and evaporation rates (92). Also, the most significant deviation from a linear relationship was noted with  $P_{H_2O}$  values greater than 15 mm. Hg - a region which was not examined in this study.

The documentation of an apparently linear and inverse correlation between IWLs and  $P_B$  verifies the observations of Hale et al. (56),

and McCutchan and Taylor (79). However, the rate of change of IWL<sub>S</sub> of  $\sim 0.58 \text{ gm./m.}^2/\text{hr.}$  for every 100 mm. Hg increase in  $P_B$  does not approach the theoretical change predicted by Miller (81) of a 3-fold increase in IWL<sub>S</sub> when  $P_B$  is reduced from 760 to 258 mm. Hg.

An objection may validly be raised that IWL<sub>S</sub> rates measured at 700 mm. Hg and those measured at 480 mm. and 258 mm. Hg  $P_B$  reflect not only a difference in total pressure but also a difference in atmospheric composition. Although differing ratios of oxygen and nitrogen were utilized at these pressures, it must also be noted that the physical properties of oxygen-nitrogen mixtures are approximately independent of the fraction of each component (30, 117). Such properties as specific heat, thermal conductivity, and viscosity show little variation when the nitrogen content of the atmosphere is reduced from 79% to 30% (table XX). Altering the nitrogen-oxygen ratios should, therefore, have a minimal effect upon the rate of insensible water loss.

The physical properties of an oxygen-helium atmosphere, on the other hand, differ markedly from those of the oxygen-nitrogen mixtures. Thermal conductivity is almost doubled, while heat capacity is reduced by 10% and density reduced by an even greater amount (13, 30). In the comparison of IWL<sub>S</sub> rates at 258 mm. Hg  $P_B$ , utilizing 100%  $O_2$  and 70:30 ratios of  $O_2:N_2$  and  $O_2:He$ , it is not surprising that rates are very similar in the  $O_2$  and the  $O_2:N_2$  atmospheres but significantly different in the  $O_2:He$  atmosphere. The 18% lower rate of skin insensible water loss which results when He is substituted for  $N_2$  may be related to the

lower average skin temperatures (fig. 14) and the lower skin temperature - ambient temperature differences ( $T_s - T_a$ ) of subjects in the helium environment. Such temperature differences had been described earlier by Epperson et al. (40), who also noted a lower rate of evaporative heat loss at ground level when He was substituted for  $N_2$ .

With the greater thermal conductivity of He, one could expect a more rapid convective heat loss to the atmosphere and a resultant lowering of the skin temperature. The lower rate of evaporative heat loss, however, would tend to balance out this increased convective loss.

The role of ambient temperature in altering  $IWL_s$  must be differentiated from its profound effect on eccrine secretion (25). In order to measure only  $W_D$  and  $W_M$ , environmental conditions must be selected in which  $W_{T_s}$  and  $W_{T_i}$  do not occur (fig. 1). There is general agreement that a mean skin temperature at or above  $34.2^\circ$  C. will lead to thermal sweating in the resting man (4, 60). Kerslake et al. (65) have shown that, below an ambient temperature of  $28^\circ$  C., the nude resting subject will not sweat. Their data also suggest that the rate of skin insensible perspiration rises linearly with increases in  $T_a$  below the sweating threshold.

Measurements of sweating thresholds on a regional anatomical basis have, however, indicated that a few areas such as the dorsum of the foot and the lower calf have a threshold as low as  $28^\circ$  C.  $T_a$  and are the first areas of eccrine activity to be recruited when the ambient temperature rises (60). One is forced to conclude, therefore, that at ambient temperatures above  $26^\circ$  C., one cannot always exclude the presence of  $W_{T_i}$ ,



however small it may be.

When one examines the effects of increases in  $T_a$  upon  $IWL_S$  rates in this study, it is immediately apparent that a consistently positive correlation is present. It is also clear that the rates of change of  $IWL_S$  with changes in  $T_a$  are not consistent. At 258 mm. Hg  $P_B$  the rate of change of  $IWL_S$  is  $+ 0.45 \text{ gm./m.}^2/\text{hr.}$  for every  $1^\circ \text{ C.}$  increase in  $T_a$  over the entire range of  $T_a$  and over the entire range of  $P_{H_2O}$  (fig. 10). On the other hand, at 700 mm. Hg  $P_B$  the rate of increase of  $IWL_S$  is only  $+ 0.27 \text{ gm./m.}^2/\text{hr.}$  from  $20^\circ$  to  $24^\circ \text{ C.}$   $T_a$ , while the rate increases to  $+ 0.72 \text{ gm./m.}^2/\text{hr.}$  from  $24^\circ$  to  $28^\circ \text{ C.}$   $T_a$ .

Here, one is presented with the first clear instance of an interaction between two environmental variables,  $T_a$  and  $P_B$ , in their influence upon skin insensible water loss. There is no doubt that the total barometric pressure can exert a direct effect upon the subjective appreciation of ambient temperature, as well as a measurable effect upon such parameters as skin temperature.

Throughout the studies there were far fewer complaints of  $20^\circ \text{ C.}$   $T_a$  being too cold and  $28^\circ \text{ C.}$  being too warm at reduced barometric pressures than at ground level. Shivering was never noted at  $20^\circ \text{ C.}$   $T_a$  at altitude, while it did occur at ground level; sweating was not observed at  $28^\circ \text{ C.}$   $T_a$  at altitude, but was occasionally detected at ground level. At the same time, average skin temperatures were consistently higher for a given  $T_a$  at 258 mm. Hg than at 700 mm. Hg  $P_B$  (fig. 14). It is probable that the rarefied atmosphere at 258 mm. Hg resulted in less convective heat loss while fostering an increased evaporative heat

loss (30, 74, 81). In the ambient temperature range below sweating threshold, the decrease in convective loss outweighs the increased evaporative loss, resulting in a skin temperature which is higher than at ground level. At or above the sweating threshold, enough skin water is available so that the increased evaporative heat loss outweighs the reduced convective loss, and the skin temperature should then fall below that of ground level. This fall in skin temperature with lower  $P_B$  has been observed by Taylor and Buettner (113) and by McCutchan and Taylor (79) who experimented above  $28^{\circ}$  C.  $T_a$ .

In the current study, the relationship of ambient temperature to average skin temperature roughly parallels the relationship of skin temperature to skin insensible water loss (compare figs. 14 and 15). Even at 700 mm. Hg  $P_B$ , however, the relationship between  $T_a$  and  $T_s$  is linear, and an increased rate of change of  $T_s$  was not noted above  $24^{\circ}$  C.  $T_a$ . Because of these parallels, it is tempting to speculate that skin temperature is an important mediator of the effects of both ambient temperature and total pressure upon rates of IWL<sub>g</sub>. A discussion of this possibility will be continued below.

The final environmental factor explored in this study, wind velocity, also exhibits a complex interaction with other environmental variables in the determination of rates of skin insensible water loss. At lower airflows, in the region of predominantly free convective cooling, this interaction is minimal, and the influence of  $P_B$  and  $P_{H_2O}$  is not greatly altered. When the wind speed increases sufficiently to cause significant forced convective cooling, however, the influence of both

$P_B$  and  $P_{H_2O}$  upon  $IWL_S$  rates diminishes rapidly.

Unfortunately, most of the determinations of  $IWL_S$  in the literature have neglected the effects of  $V$  or have studied its effects at ambient temperatures above the sweating threshold (79), or in pressure suits (128). The data of Taylor and Buettner (22, 113) demonstrated a rough correlation between wind speed and total evaporative water loss at any specific skin temperature. As the wind speed increased from 2 to 5 km./hr., water loss rates at a specific skin temperature tended to group together regardless of  $P_{H_2O}$ .

Observations, here and in several other studies, indicate that increased air movement tends to lower skin temperature while increasing  $IWL_S$  at a given  $T_a$ . This lowering of skin temperature (fig. 14) may be directly related to the increased evaporative rate and increased evaporative heat loss. Gagge, however, suggested that surface vasoconstriction may mediate the fall in  $T_s$  at higher wind speeds (59).

This alteration in  $T_s$  by rapid airflows may be, at least in part, responsible for the diminished influence of changes in  $P_B$  and  $P_{H_2O}$  upon  $IWL_S$  rates under these conditions. The tendency for a low  $P_B$  to be associated with an elevated average skin temperature may be counteracted by the higher wind velocities and the resultant increase in forced convective cooling (30). The more rapid air flows over the skin surface may also tend to increase the  $P_{H_2O}$  gradient between the skin and air, resulting in an increased rate of evaporation and, perhaps, a concomitant increase in diffusion of water vapor. At high

values of  $V$  the air evaporative capacity may increase so greatly that differences in  $P_{H_2O}$  assume progressively lower significance to skin water loss rates (92).

In an examination of each of these environmental variables and its effect upon skin IWL, the close correlation of average skin temperature changes with changes in both the environmental variables and IWL<sub>S</sub> rates has been noted. Birch and Winsor (27), experimenting with excised human skin in 1944, noted that as the temperature of the skin was increased the rate of water loss increased proportionally. Other studies have confirmed this relationship but have also demonstrated a significant degree of residual variation when IWL<sub>S</sub> rates are plotted solely against  $T_s$  (3). Taylor and Buettner (113) then pointed out, in 1953, that many other environmental variables could affect skin water loss somewhat independently of skin temperature.

The fact that  $T_s$  does not correlate completely with IWL<sub>S</sub> rates, however, should not detract from its obviously important involvement in the skin insensible water loss process. The major question remaining unanswered relates to whether the alterations in skin temperature actually cause the changes in IWL<sub>S</sub> rates, or whether the physical processes which alter IWL<sub>S</sub> rates also alter skin temperature in a parallel manner. Since diffusion and evaporation are involved in skin insensible water loss, it seems likely that  $T_a$  would have some direct effect on both of these processes. At the same time, physical changes in the environment, such as increased wind speed, may cause skin temperature to decrease while IWL<sub>S</sub> increases. Such changes

provide strong evidence that the relationship of  $T_a$  to IWL<sub>S</sub> is not always a consistent one, and that environmental variables may cause these two measurements to move in opposite directions. Viewing all of the evidence, one must conclude that  $T_a$  does exert some direct influence on IWL<sub>S</sub> rates as do other environmental factors which alter the rates of diffusion and evaporation. One must also conclude that these other environmental factors exert a direct effect on  $T_a$ , just as they do upon IWL<sub>S</sub>. By changing convective heat losses or evaporative heat losses,  $T_a$  is caused to vary in a direction often parallel to rates of IWL<sub>S</sub>.

The correlation of effective wall temperature ( $T_{ew}$ ) with measured rates of IWL<sub>S</sub> has been pointed out in the stepwise multiple regression analysis of environmental factors shown in table XIV. Of all the quantifiable features of the environment studied,  $T_{ew}$  consistently demonstrated the closest relationship to rates of skin insensible water loss. Since this term must take into account changes in many ambient parameters such as black-globe temperature and ambient temperature, as well as several coefficients which vary with ambient conditions, it is not surprising that a significant correlation with rates of IWL<sub>S</sub> does appear.  $T_{ew}$  not only gives an indication of the total heat load on the experimental subject, but also is influenced by the subject's own surface temperature.

If one compares figure 14, which shows the relationship of average skin temperature to ambient temperature, with figure 49, which shows the relationship of average skin temperature to  $T_{ew}$ , a major difference

is seen. For any given ambient temperature, a decrease in  $P_B$  is associated with a higher  $T_S$ . For any given  $T_{e_w}$ , however, a decrease in  $P_B$  is correlated with a lower  $T_S$ .

The marked increase in heat loss through radiation in the experimental subjects at reduced  $P_B$  is reflected in the great increase in  $T_{e_w}$  which is also seen. This increase in radiative heat load and in  $T_{e_w}$  is sufficient to completely mask the smaller rise in subject skin temperature which also occurs at reduced  $P_B$ . Thus, any  $T_{e_w}$  at reduced  $P_B$  may actually be associated with a lower  $T_S$  when compared with a normal  $P_B$ .

Although an important influence of five environmental variables upon rates of skin insensible water loss has been demonstrated in this study, the specific physical or physiologic mechanisms which cause the changes in IWL rates remain to be defined. The diffusion and evaporation theories of Buettner and Taylor are still the most widely accepted, although they have been challenged, at least in part, by Goodman and Wolf (50) and Peiss and Hertzman (92).

In this discussion, it must be remembered, skin insensible water loss is considered to have two major components when thermal sweating is not activated -  $W_D$  and  $W_M$ . The former corresponds to the diffusional water loss described by Burch, Buettner, Pinson, and others. Although this water is thought to diffuse directly through the layers of the epidermis, it would not be impossible for a very small percentage to diffuse out of the walls of eccrine sweat ducts and other skin appendages. The latter component ( $W_M$ ) is composed of water that is

actively secreted by constantly functioning eccrine and apocrine sweat glands that are not under thermal control (61, 99). Like  $W_D$ , rates of  $W_M$  vary over different skin areas.

Although one can talk theoretically about  $W_D$  being the only component of transepidermal insensible water loss and proceed to measure only  $W_D$  in an attempt to define its mechanism and controls, this approach will not provide any information about the rates of skin fluid loss from the whole animal as they actually occur.  $W_M$ , as well as  $W_D$ , must be evaluated on a total-body basis.

Having agreed that  $IWL_S$  has two major components, one can logically progress to question whether  $IWL_S$  may have two mechanisms of control. The component of water loss provided by  $W_M$  represents active glandular secretion, therefore, the process of diffusion will be of lesser importance. The secreted water must be vaporize, however, and be carried away from the body surface; so, the process of evaporation assumes great importance.

The major component of skin water loss provided by  $W_D$  will depend upon the processes of both diffusion and evaporation - whether this water diffuses directly through the many layers of the epidermis, or from the sweat ducts (as suggested by Goodman). Regardless of the route through the skin to the surface, the rate of diffusion will depend upon physical parameters in the immediate environment.

Examining the equations which describe the processes of diffusion and evaporation, one can see that all of the environmental parameters

investigated in this study play an important role.

In the case of diffusion (m):

$$m \approx \frac{1.75 Q \left( \frac{T_a}{273} \right) \left( \frac{760}{P_B} \right) \left( \frac{P_{H_2O_s}}{T_s} - \frac{P_{H_2O_a}}{T_a} \right)}{\frac{1}{F} \left[ R_s + C V^n \left( P_o / P_B \right) N \right]} \quad (13)$$

In this process the environmental variables,  $T_a$ ,  $P_B$ ,  $P_{H_2O}$ , and  $V$  are all important in determining the rate. ( $Q$ ,  $F$ , and  $C$  are constants, while  $R_s$  represents the resistance of the skin.)

In the case of evaporation:

$$E \approx C (P_{H_2O_s} - P_{H_2O_a}) (1 + V/k) (1 - P_B/K) \quad (14)$$

(96)

where  $C$  is a constant dependent upon  $T_a$ , and  $k$  and  $K$  are also constants. In this process, also, the environmental variables  $T_a$ ,  $P_B$ ,  $P_{H_2O}$ , and  $V$  are all important in determining the rate. In both equations, many of the so-called constants are directly influenced by atmospheric gas composition, so that GC also plays a role in these processes.

The introduction by Mole (82) of the concept of relative humidity of the skin provided an expression of the water content of the surface layer of the skin expressed as a percentage of the maximum content, the maximum being a homogeneous thin layer of water over the entire surface. Peiss and Hertzman (92) speak of the skin R.H. as a measure of the relative amount of water available for diffusion and evaporation.



Changes in the rate of  $W_D$  can be caused by alterations in the R.H. or state of hydration of the stratum corneum which are independent of skin temperature, or by changes in the skin resistance to diffusion.

Although the concept of skin relative humidity is a useful one in talking about the amount of water available for IWL<sub>G</sub>, it has been pointed out that it fails to quantitate the mechanisms involved, and is essentially an artifact whose value is determined by the evaporative rate and the vapor pressure differences along the route of diffusion.

When only the  $W_M$  component of IWL<sub>G</sub> is considered, one is dealing with a glandular secretion whose production is not influenced by environmental changes in  $T_a$ ,  $P_B$ ,  $P_{H_2O}$ ,  $V$ , and  $GC$ . Only after secretion and exposure to the ambient air do environmental factors influence its disappearance from the human body through evaporation (equation 14). Skin relative humidity and skin resistance to diffusion play no role in the rate of water loss.

This is not the case with  $W_D$ , which must first diffuse to the skin surface or to a water vapor-air interface in order to evaporate. Ambient conditions of  $T_a$ ,  $P_B$ ,  $P_{H_2O}$ ,  $V$ , and  $GC$ , influence  $W_D$  as it diffuses and as it evaporates (equations 13 and 14).

In the case of  $W_M$ , the efficiency of evaporation may or may not act as the rate-limiting step. In environments of low airflow, low temperature, and high  $P_{H_2O}$ , water may be delivered to the skin surface by eccrine glands at a rate greater than the maximum evaporative capacity of the surrounding air. The water may then spread across the skin

surface and increase the area available for evaporation, may be absorbed by the skin (diffuse into the epidermis), or may run off the skin. If the evaporative capacity of the air is increased steadily, a point will be reached where all of the eccrine secretion evaporates almost immediately, and the efficiency of evaporation will no longer be the rate-limiting step. Rather, the rate of secretion of water will be rate-limiting.

In the case of  $W_D$ , a similar but more complex situation may prevail. Here, both the rate at which water vapor reaches the skin surface and the rate at which it can evaporate are extremely variable and are regulated by environmental changes. Either step may be rate-limiting, assuming that the rate of delivery of water is not always in excess of the rate of evaporation. In some environments diffusion will deliver a smaller amount of water vapor than the evaporative capacity of the air can handle, and the diffusion process will be rate-limiting; in other situations diffusion may deliver an amount of water vapor that exceeds the evaporative capacity of the air, and the evaporative process will become rate-limiting.

The accumulation of water within the epidermis because evaporation is the rate-limiting process may be a very common phenomenon. As discussed by Mole (82), the frequent observation that the wetness or R.H. of the skin increases as the humidity of the air increases is related to the fact that diffusion or secretion of water continues without the water being added to the evaporative loss or running off the skin. Mole goes on to hypothesize that, with constant convection and air

temperature, an increase in air humidity will temporarily decrease the loss of skin water vapor by evaporation until the continuing diffusion of water from the tissues beneath the epidermis raises the skin humidity and subsequently boosts the evaporative rate.

Although a division of the transfer of water from the epidermal interior to the surrounding air into the two processes of diffusion and evaporation may be an artificial one in some circumstances, it is nonetheless a very useful one. The location of the liquid water-water vapor interface may lie at various levels within the epidermis or may lie on the skin surface, depending upon the R.H. of the skin, the activity of eccrine and apocrine glands, the repenetration of water into the skin, the evaporative capacity of the environment, and several other factors (17).

The so-called barrier membrane located deep within the epidermis, (principally at the levels of the stratum granulosum and stratum compactum (89, 107), which inhibits the free flow of water to the surface, does not necessarily demarcate the liquid-vapor interface. While diffusion takes place through this barrier membrane, evaporation may commence at any level at or above the membrane where a liquid-vapor division occurs.

Barrer (6) has examined the manner in which diffusion through solid membranes can take place, and has given the name "activated diffusion" to the process by which a substance may diffuse through the pores in a lattice of complex organic molecules. Such diffusion

is facilitated by temperature elevations, which increase the activity of the diffusing molecule and increase the average pore size in the membrane. Passage of water molecules through the barrier membrane of the epidermis appears to fit the process of facilitated diffusion.

The diffusion coefficient of the barrier membrane and its relationship to water vapor pressure is still a matter of dispute. King (66) demonstrated that, in the transport of substances through keratin membranes, the diffusion coefficient itself can vary with the concentration of the diffusing substance. The barrier zone of normal human epidermis has also been shown to exhibit an absorption isotherm and hysteresis effect in its interaction with water vapor. Mali (73) has shown, however, that very little water is absorbed by the barrier layer until an ambient R.H. above 70% is reached, and that the permeability constant varies only slightly over a wide range of R.H. values. The permeability of the barrier-zone epidermis of the trunk was roughly proportional to the difference in  $P_{H_2O}$  between the two sides of the membrane and inversely proportional to the thickness of the membrane.

This finding, as well as the water-vapor data accumulated in the current study and by Zollner and Thauer (132), does not support the contention that the effect of increasing  $P_{H_2O}$  on skin insensible water loss is negligible because of an absorption isotherm in the barrier membrane (50).

Subject-to-subject variations in  $IWL_S$  rates under identical environmental situations are most likely related to differences in epidermal

structure, with resulting differences in permeability. No firm evidence for physiologic adjustment of permeability is available.

The efficiency of the water barrier zone of the epidermis varies considerably in different people and in different parts of the body, with significantly increased permeability in the palms and soles and minimum permeability in the chest and abdomen (92, 132). Some measurements indicate that the permeability of palmar skin to water is more than 20 times that of abdominal skin (92). This represents a decrease in barrier efficiency from 99.7% to 92.5% in its inhibition of free water passage.

Barrier efficiency drops even further when the skin is diseased and the architecture disrupted. In addition to thermal or chemical burns, diseases such as psoriasis, ichthyosis, and erythroderma may cause a 300% increase in skin insensible water loss (43, 54, 105, 108). In extreme cases, the loss of water through the skin may become life-threatening. In such cases, barrier efficiency may fall below 20% and water loss rates exceed  $200 \text{ gm./m.}^2/\text{hr.}$  (83, 107).

It is more difficult to relate intrasubject variations in IWL<sub>S</sub> rates for replicate runs to changes in epidermal architecture or to changes in barrier membrane efficiency. Such intrasubject variations have been noted by other experimenters irrespective of measurement technics used (14, 50, 64, 88, 114). Since measurements occur only a few hours apart, one would not expect significant physical alterations within the skin in so short a time. These intrasubject changes in IWL<sub>S</sub> rates, therefore, suggest that some physiologic adjustments could be

acting to influence skin water loss within limits.

#### Fluid Balance studies

The accuracy of any fluid - or weight - balance study rests almost completely with the successful collection of all sources of weight loss and the accurate measurements of all intake and output. A measure of this accuracy is the closeness with which the values for total intake and total output agree, taking into account changes in body weight.

In this study an average difference of 300 gm. was noted over the first seven experiments with measured grand total outputs always lower than total intakes. This lower-than-expected output can be accounted for in several ways. In the first place, the grand total output is computed from  $W_0 + W_{e1}$ . As such, it includes all routes of weight loss, both sensible and insensible, with  $W_G$ . Considering the average activity of an experimental subject during a 24-hour period,  $W_G$  would account for another 130 gm. of weight loss (table XI), bringing the intake-output difference down to 170 gm.

In the second place, the rate of skin insensible water loss ( $W_{e1}$ ), from which the 24-hour total IWL<sub>S</sub> is computed ( $W_{e1t}$ ), represents the rate of water loss associated with minimal metabolic activity and with the subject lying flat on the metabolic scale. Over the entire 24-hour period, the subjects actually averaged a greater degree of activity, so one would expect their true value of  $W_{e1t}$  to be higher than that estimated from  $W_{e1}$ . Some thermal sweating was noted, with increased activity between measurement periods, substantiating the rise in skin water loss.

The effect of total barometric pressure on almost all aspects of weight balance was not anticipated (table XXI). The consistent increase in total intake at 258 mm. Hg  $P_B$  and the consistent decrease in both urine-feces output and grand total output at this reduced pressure are similar to changes noted in acute mountain sickness. In the latter situation, however, reduced  $P_{O_2}$ , rather than reduced  $P_B$ , is thought to be the most important etiological factor (58, 80, 94, 106, 110). Multiple studies at the top of Pike's Peak, Colo. (alt. 14,100 ft.) have shown a near-normal or negative fluid balance in non-acclimatized subjects (36, 58, 80). Similar results were noted in athletes taken to the Andes for high-altitude training (31). In contrast to this, Galeotti and Signorelli (45) noted that subjects, in the Alps, demonstrated a positive water balance under resting conditions but a negative balance under active climbing conditions. The observations of Singh et al. (106) at altitudes from 11,000 to 18,000 ft. confirmed that subjects developing acute mountain sickness experienced a significant antidiuresis with weight gain during the first 6 to 96 hours of exposure.

In all of these studies hypoxia as well as reduced  $P_B$  were present, making it impossible to separate the individual effects of these two environmental factors. A negative water balance has also been noted on prolonged space flights of the Gemini and Apollo programs, where astronauts are subjected to weightlessness as well as to a lowered  $P_B$  (47, 48). An increased fluid output is accompanied by a decreased thirst, so that the fluid deficiencies are not made up.

The slight increase in total insensible water loss with reduced  $P_B$  noted in this study was attributable to the balancing of an increased  $IWL_S$  with a diminished  $IWL_R$ . If a reduced  $P_{O_2}$  had been present, then  $IWL_R$  would also have increased with reduced  $P_B$ , and  $IWL_T$  would have shown a marked increase.

As one would predict, a decrease in  $P_{H_2O}$ , with all other environmental parameters held constant, resulted in a significant increase in all sources of water loss and also in fluid intake (table XXI). The significant rise in  $IWL_T$  with falling  $P_{H_2O}$  was related to dramatic increases in both  $IWL_S$  and  $IWL_R$ . The increasing insensible water loss was accompanied by a decreasing loss of water through urine and feces.

With an increasing  $T_a$  one would also anticipate an increase in  $IWL_T$  because of an increase in both  $IWL_S$  and  $IWL_R$ . The increase in insensible water loss with rising temperature was also accompanied by a fall in sensible loss through urine and feces. The significant increase in fluid intake with a rise in  $T_a$ , despite the absence of thermal sweating, demonstrates the importance of temperature in estimating fluid requirements, no matter what the temperature range.

Of all the environmental factors studied, gas composition appeared to have the least effect on overall fluid balance (table XXI). Only  $IWL_S$  and, concomitantly,  $IWL_T$  were influenced by the substitution of He for  $N_2$ , and values for total intake and output were not significantly altered. Because of the similar physical properties of pure oxygen and oxygen-nitrogen mixtures, one would not expect to see differences in evaporative water loss or total water loss unless physiologic



adjustments played a major role. The effects of He on  $IWL_G$  and  $IWL_T$  can be related to its markedly different physical properties.

The attempt to calculate skin insensible water loss by the indirect approach of a weight-balance equation was not altogether successful. In the 27 experiments in which the calculation of  $W_{e2t}$  was made, values of  $W_{e2t}$  were almost always higher than the measured  $W_{e1t}$  values. In only one instance, however, did the difference in the two determinations exceed 400 gm. In 24 of 27, the difference was less than 300 gm./24 hr.; in 19 of 27, less than 250 gm./24 hr.; and in 12 of 27, less than 200 gm./24 hr.

The higher rate of skin water loss determined through the use of the weight-balance equation may again reflect an actually higher average rate of skin water loss over a 24-hour period when the subject is not always in the resting state. Sweating during physical exertion would drive the skin water loss to a much higher level than would be anticipated from the resting measurements of  $W_{e1}$ .

The use of an indirect method of calculating skin insensible water loss would have broad application where elaborate equipment to measure  $IWL_G$  directly is not available or is not logistically usable. Caution must be exercised in the interpretation of these indirect results, however, since the influence of environmental variables on the rates of water loss is not as easily discerned with this method.

The relationship of environmental variables to respiratory water

loss rates ( $IWL_R$ ) has been explored since 1904, when Foa (as cited in Marshall and Specht, 75) suggested that lung water loss was reduced at high altitude. This finding was substantiated by Guillemard et al. (55) in 1910. Galeotti and Signorelli (45) investigated the effects of the temperature and humidity of inspired air and found that increasing the inspired humidity significantly reduced the respiratory water loss. Newburgh and Johnson (87) concluded that respiratory water loss was controlled simply by the environmental conditions and by the lung ventilation rate. Other investigators (77, 124, 131) later showed that additional factors, such as the amount of respiratory dead space and the transit time of air through the lung, play a limited role in the determination of  $IWL_R$ .

Disagreement has been frequent as to whether the expired air is saturated with water vapor. Measurements by Corlette (37), Buettner (23), and Pfeiderer and Less (93) originally indicated that this air was saturated. Studies by Seeley (104), Christie and Loomis (33), Burch (29), and McCutchan and Taylor (77) all concluded that the expired air was only 80% to 90% saturated for most ambient conditions. A consideration of the data available has led most current investigators to conclude that 100% saturation rarely occurs.

The data presented in this study, concerning the rates of  $IWL_R$  and the influence of environmental variables upon these rates, are in close agreement with the conclusions of other investigators (1, 29, 75, 131). The significant increase in  $IWL_R$  with a decrease

in ambient  $P_{H_2O}$  or an increase in  $T_a$  has been documented by McCutchan and Taylor (77), Burch (29), and Seeley (104). At low values of  $P_{H_2O}$  and high values of  $T_a$ , the inspired air is physically capable of picking up and holding more water vapor as it passes through the respiratory tract and approaches saturation. The quantity of water that can be added and held by the air is directly related to its degree of saturation before entering the lungs, since its saturation upon leaving the respiratory tract is held to 80% to 90%. Assuming a constant respiratory ventilation and a constant dead space and air transit time, the rate of respiratory water loss should be directly related to the R.H. of the inspired air, regardless of ambient temperature or water vapor pressure. Such a relationship was indeed observed in this study (fig. 25).

This relationship does not exist between skin insensible water loss and R.H. (fig. 26), where changes in  $T_a$  result in a shift of the y-intercept. It is clear that  $T_a$  has an important influence upon IWLs rates - an influence separate from its effect on ambient air saturation.

The observations of Foa and others that IWL<sub>R</sub> rates were reduced at high altitude have been recently amplified and quantified by Marshall and Specht (75) and by Wortz et al. (131). The later study concluded that decreases in minute volume with reduction in  $P_B$  account for the accompanying reduction in respiratory water loss. A further

conclusion was that  $IWL_R$ , calculated in grams per liter of expired gas, did not vary with total pressure, while minute volumes decreased as much as 33% at 180 mm. Hg  $P_B$ . Rates of  $IWL_R$  fell from an average of 7.2 gm./m.<sup>2</sup>/hr. at 760 mm. Hg, to 5.8 gm./m.<sup>2</sup>/hr. at 180 mm. Hg  $P_B$ .

A significant reduction in minute volume at reduced  $P_B$  had been predicted by Jaeger and Otis (63) and Fenn (42) based on the fact that the work of breathing is reduced and the airway turbulence and resistance are lowered as the barometric pressure falls and atmospheric gases are rarefied.

In this study, pulmonary ventilation decreased by 10% from 538 to 485 liters/hr. with a decrease in  $P_B$  from 700 to 258 mm. Hg. This drop is smaller than would have been predicted from other work (131), possibly because of the mechanical resistance in the outflow circuit of the breathing apparatus with its large Drierite canister. The variations in rate of  $IWL_R$  with lower barometric pressure are directly proportional to this change in pulmonary ventilation, and also approximately a 10% reduction over the full range of  $T_a$  and  $P_{H_2O}$  measurements.

Total insensible weight loss, being composed of  $IWL_S$ ,  $IWL_R$ , and  $IWL_G$ , may range from 500 to almost 1,100 gm. in a 24-hour period, even when thermal sweating does not occur. Thus,  $IWL_T$  may account for almost 50% of the total sensible and insensible body weight loss in a day, especially when a high  $T_a$  and  $V$  are combined with a low  $P_B$ .

and  $P_{H_2O}$ . Since a change in water vapor pressure from 14 mm. to 4 mm. Hg can result in a 300 gm./day increase in water loss, and a change in ambient temperature from  $20^{\circ}$  to  $8^{\circ}$  C. can also cause a 300 gm./day increase in insensible water loss, it is clear that environmental variations which fall within or very close to the recognized "comfort zone" can result in major alterations in body water balance if fluid intake is not properly adjusted.

Although some investigators have stated that  $IWL_R$  usually comprises almost 50% of total insensible water loss, this figure was found to be exaggerated in the current study. Skin insensible water loss formed the major component of  $IWL_T$  under all conditions measured, and never fell below 53% of the total.  $IWL_R$  accounted for as little as 25.5% of  $IWL_T$  under environmental conditions featuring high  $P_{H_2O}$  and low  $P_B$  and  $T_a$ , and increased to almost 44% under conditions of low  $P_{H_2O}$ , high  $P_B$ , and average  $T_a$ .

It is important to recall that, although the influence of  $P_{H_2O}$  and of  $T_a$  upon both  $IWL_S$  and  $IWL_R$  is in the same direction, the influence of  $P_B$  on each of these two routes of insensible water loss is directly opposite. At very low values of  $P_{H_2O}$ ,  $IWL_S$  decreases so rapidly and  $IWL_R$  increases so rapidly with increasing  $P_B$  that, at  $P_{H_2O}$  values lower than those studied here, respiratory water loss should exceed skin insensible water loss.

Development of signs and symptoms:

Environmental criteria for human comfort, as established in the ASHRAE index, indicate very little effect of relative humidity or water vapor pressure, especially at their lower ranges. Only above a 70% R.H. is the ambient temperature of maximum comfort shifted slightly (2). A standard Aircraft Environmental Limit Chart (121) establishes a "comfort zone" which includes R.H. down to 10%, and environmental design charts developed for NASA have indicated an "unimpaired performance zone" which includes water vapor pressures as low as 5 mm. Hg (51). None of these environmental indices take into account major changes in total pressure, atmospheric gas composition, or airflow (90).

In recent years, the United States Air Force has noted significant dehydration, together with increased fatigue, in crews flying multiple transpacific missions in high-flying pressurized aircraft like the C-141. Discomfort and dehydration among the sick and injured on medical evacuation flights have also been observed. A cabin atmosphere which features a  $P_{H_2O}$  of less than 3 mm. Hg is a feature of these aircraft, and nasal stuffiness, lip chapping, and occasional eye irritation have been frequently reported. Such discomfort also occurs on long flights on commercial jet liners.

Similar symptoms affecting the eye and nose have been reported by American astronauts in Gemini and Apollo flights. A low-humidity

environment has been established in these spacecraft, but it is not certain whether it is the low  $P_{H_2O}$  or the increased oxygen partial pressure which is primarily responsible for the adverse effects.

Few serious attempts to quantitate the effects of environmental variables on human sign and symptom development have been carried out in these situations where environmental effects are prominent (46). The use of any type of quantitative index to evaluate subjective and objective changes is fraught with difficulties. A clear set of criteria for assigning numerical values to signs and symptoms must first be established, and then observers must be trained to relate these numerical values to signs and symptoms uniformly and consistently.

In this study, careful training of subjects by medical experts and repeated drilling with the subjective and objective evaluation sheets did produce a high degree of uniformity and consistency. This was reflected in the reproducibility of the data and the clear trends which developed when environmental parameters were altered.

The finding that the subjective evaluation, or Symptom Index, was more sensitive to environmental alterations than the objective evaluation, or Sign Index, was not unexpected. An individual is often able to notice subtle changes in his own feelings or health before objective changes are apparent. A nose will feel stuffy before marked mucosal edema is evident to others; a throat will feel

scratchy before significant inflammation develops. That the subject objective evaluations should be more sensitive than the physician objective evaluations was not completely anticipated, although several possible explanations for this phenomenon can be presented.

The final physician evaluation was performed some minutes after subjects emerged from the environmental chamber, and at this time the subjects, themselves, noted some improvement in signs and symptoms. Subjects were frequently aware of the symptoms claimed by the individual they were examining and could thus be biased in their evaluation of physical findings. (The physicians were not aware of the subjects' complaints)

Total barometric pressure, water vapor pressure, and ambient temperature all exerted a significant effect on the development of both signs and symptoms in the experimental subjects. Although four studies were run substituting 100% O<sub>2</sub> and O<sub>2</sub>:He atmospheres at 258 mm. Hg P<sub>B</sub>, no significant alteration in the Sign Index could be detected. A small, but not statistically significant, increase in the Symptom Index in 100% O<sub>2</sub> and a small decrease in this index in O<sub>2</sub>:He were noted, however.

A failure of the high oxygen atmosphere to be a significant augmenter of sign and symptom development has a number of explanations.

In the first place, one could conclude that it is the low humi-



dity rather than the  $O_2$ , itself, that is the culprit in artificial environments where dry oxygen is utilized. On the other hand, one may note that 100%  $O_2$  atmospheres in this study provided a  $P_{O_2}$  of only 258 mm. Hg, which is just 60% greater than normal air and 44% greater than the  $O_2:N_2$  atmosphere provided. If oxygen tensions had been higher, a more dramatic change in sign or symptom development might have been seen.

The interaction of  $P_B$  and  $P_{H_2O}$  in sign and symptom development is apparent in the 48-hour studies, alone, and in the grouped data for all experiments of 24-hour or longer duration. This interaction is of prime importance when one is selecting the minimum acceptable water vapor level for an environment in which the total pressure may be reduced; i.e., a spacecraft. Whereas at ground level, or 700 mm. Hg  $P_B$ , a water vapor pressure of 6.5 mm. Hg would be compatible with only a slight increase in signs and symptoms; at 27,000 ft., or 258 mm. Hg  $P_B$ , signs and symptoms would have increased markedly at 6.5 mm. Hg  $P_{H_2O}$ . At this reduced  $P_B$ , a  $P_{H_2O}$  no lower than 9 mm. Hg would be required to prevent this increase of subjective and objective abnormalities. This important effect of  $P_B$  is pointed out by the fact that the Symptom Index changes only from -0.64 to -0.68 when  $P_{H_2O}$  is reduced from 9 to 6.5 mm. Hg at 700 mm. Hg  $P_B$ . At 258 mm. Hg  $P_B$ , on the other hand, the Symptom Index jumps from -0.71 to -0.88 for this same fall in  $P_{H_2O}$ .

The influence of ambient temperature upon sign and symptom development is mediated by direct thermal effects, as well as by drying of exposed surfaces. When the average skin temperature falls below  $31^{\circ}\text{C}$ ., a clear sensation of cold usually develops; and when the  $T_s$  falls below  $30^{\circ}\text{C}$ ., shivering usually ensues. At the opposite extreme, a sensation of uncomfortable warmth usually does not develop until the skin temperature rises above  $35^{\circ}\text{C}$ . (125).

At total pressure of 258 mm. Hg, the sign-symptom indices showed very little change over the ambient temperature range from  $20^{\circ}$  to  $28^{\circ}\text{C}$ . At ground level, or 700 mm. Hg  $P_B$ , however, a significant change in both the Sign-Symptom Index and the Symptom Index occurred between  $24^{\circ}$  and  $20^{\circ}\text{C}$ . Subjects complained of being cold at  $20^{\circ}\text{C}$ . only at ground level, and shivering was noted on a few occasions. An increase in nasal stuffiness with some coryza developed in most subjects - most likely a vagal response to feelings of coldness.

This major difference in response to the  $20^{\circ}\text{C}$ . environment at the two divergent total pressures is most likely related to the greater convective heat loss at 700 mm. Hg in a denser atmosphere. The average skin temperature at 700 mm. Hg  $P_B$ ,  $20.6^{\circ}\text{C}$ . was as low as  $29.9^{\circ}\text{C}$ .; while at 258 mm. Hg  $P_B$ ,  $20.9^{\circ}\text{C}$ ., skin temperature averaged  $31.5^{\circ}\text{C}$ . Similarly the  $T_{ew}$  rose from  $20.0^{\circ}\text{C}$ . to  $26.0^{\circ}\text{C}$ . when  $P_B$  was changed from 700 mm. to 258 mm. Hg. The difference in the timecourse of symptom and sign development over 48 hours is

most dramatically illustrated in the comparison of 14 mm. with 4 to 5 mm.  $P_{H_2O}$  atmospheres. At the elevated water vapor pressures, the sign and symptom indices changed only slightly over the first 12 hours and then held at a constant level. At the extremely low levels of  $P_{H_2O}$ , the indices changed rapidly through the first 20 hours of exposure and then remained remarkably constant. In almost all cases, sign and symptom development was more rapid at 258 mm. than at 700 mm. Hg  $P_B$  and plateaued at a greater level.

It is important to note that signs and symptoms did not continue to develop or to worsen throughout the 48-hour exposure periods, even at the very low levels of  $P_{H_2O}$ . The leveling off after the first 20 hours may represent some small degree of adaptation or acclimatization, but, at the same time, it is clear that there was no tendency for signs and symptoms to diminish during the later hours of exposure. A steady-state condition persisted until the experiments were terminated; only one hour after termination, symptoms had already decreased significantly.

Note must also be taken of the fact that sign and symptom development did occur even at the high levels of  $P_{H_2O}$  (i.e., 14 mm. Hg, R.H. 66%) where one would not expect it. This phenomenon is at least partially related to certain features of the environmental chambers in which the experiments were conducted. A fairly high noise level was constantly present from large blowers and the environmental control

systems, and experimental subjects were forced to speak loudly to one another in order to make themselves understood. Because of the vocal strain, significant hoarseness and some throat irritation invariably developed in all experiments, irrespective of environmental conditions. In addition, the Beta-cloth covering of the metabolic scale and Beta-cloth sheets used on the beds caused some skin-itching, which was also reported on the subjective evaluation sheets.

Also, since the subjects were not advised, in advance, of the environmental conditions that they would be facing, there was probably a psychological attempt - either conscious or subconscious - to note some changes in their subjective or objective evaluations in order to please the investigators.

The analysis of signs and symptoms according to anatomical areas involved bringing several important points to light. In the data summaries from all experiments, the relative frequency-severity of 6 of the 9 anatomical categories differed greatly in respect to symptoms and signs. Whereas the subjects were most often bothered by nose problems, particularly stuffiness, nasal signs were reported less than signs involving the lips and eyes. On the other hand, while lip signs were most frequently noted, lip symptoms were reported by the subjects less than nasal symptoms. Only scalp, skin, and general categories maintained their same 7th, 8th, and 9th, positions in both the Sign Index and the Symptom Index.

It is interesting to note that nasal stuffiness, lip chapping, and occasional eye-burning and tearing were the most frequent complaints aboard jet aircraft, Apollo capsules, and often in forced-air heated homes. These same signs and symptoms predominated in the current study (table XVIII).

Signs and symptoms involving the nose, lips, and eyes were also most dramatically affected by alterations in those environmental parameters which increase the rate of skin insensible water loss. This was particularly evident with a lowering of  $P_B$  or  $P_{H_2O}$ . Changes in  $T_a$  were closely associated with symptom changes involving the nose and tongue in one direction (with a lowering of the  $T_a$ ), and the lips and pharynx in the other (with a high  $T_a$ ). Changes in gas composition, particularly the 100%  $O_2$  environment, were related to increases in nose, pharynx, tongue, and scalp symptoms and to lip, tongue, mouth, and skin signs.

The fact that the skin and scalp were least affected by environmental changes may be related to the length of exposure. Nonkeratinized surfaces, such as the eyes, nose, and lips, dry more rapidly, causing a rapid increase in signs and symptoms. Perhaps if exposures had been extended well beyond 48 hours, drying of skin and scalp would have been more noticeable. In an intermediate position in terms of sign and symptom development were the tongue, mouth, and pharynx. These areas were exposed only indirectly to the ambient environment

when air was inhaled, and thus did not experience the full drying effect of the atmosphere.

The failure to observe significant changes in sensory function as measured by the special vision, taste, and olfaction tests in many experiments may also be related to the lengths of exposure. Since visual acuity and olfactory changes were noted only in those studies where the most severe drying conditions existed and rates of IWL<sub>S</sub> were maximal, an exposure period of longer than 48 hours might have brought out sensory changes at more intermediate conditions of  $P_{H_2O}$ ,  $P_B$ , and  $T_a$ . That humidity levels affect the sense of smell or the production of odors has long been known in the air-conditioning industry, and several studies have suggested that high levels of  $P_{H_2O}$  increase olfactory sensitivity (68). Although tearing as measured by the Schirmer test was significantly decreased in three experiments featuring low levels of  $P_{H_2O}$ , the lack of reliability of this test makes any interpretation difficult (49).

Alterations in taste thresholds as measured by the gustometer were seen in varying environmental situations. Decreases in taste were seen in some experiments featuring either low  $P_{H_2O}$  or elevated  $T_a$ , all at reduced barometric pressure. On the other hand, the increase in taste noted in both experiments conducted in a helium atmosphere may cause speculation that the helium, itself, is responsible for this taste acuity. Whether this gas can facilitate

the diffusion of substances through the pores of taste buds or act in some way to "tune up" the taste apparatus is a matter for future investigation.

The relationship of sign and symptom development to rates of insensible water loss, especially skin insensible water loss, is a positive one (fig. 47). In environments where  $IWL_g$  is low or only moderately increased, however, increases in the Sign-Symptom Index are small (fig. 48). This relatively small increment of sign and symptom change may be related to the ability of exposed skin and mucous membranes to adequately compensate for slower rates of water loss and thus resist surface dehydration. Fluid may be transferred from the underlying tissue at a sufficient rate to balance the surface losses. As rates of skin water loss increase further, rehydration of surface tissue may not keep up with the rate of loss, thus accelerating the development of signs and symptoms. With rates of  $IWL_g$  greater than  $8.5 \text{ gm./m.}^2/\text{hr.}$ , the Sign-Symptom Index increased markedly with small increases in  $IWL_g$  rates.

In summary, it is clear that all five environmental parameters examined in this study can exert a significant effect on skin and total insensible water loss, on total fluid balance, and on subjective and objective measurements of comfort. One does not need to seek extreme ambient conditions that lead to marked discomfort, significant thermal sweating, or pronounced dehydration in order

to observe and quantitate these environmental influences. Even within the generally accepted "comfort zones," these influences are evident.

The quantitative analysis of routes of insensible water loss from the human body, as influenced by environmental variables, can be correlated with overall fluid balance and with sign and symptom development. In this way a true picture of man's interaction with his environment can be defined (52), and accurate predictions for differing combinations of ambient parameters can be accomplished. Such associated factors as fluid requirements, urine and feces output, water loads on air-conditioning equipment, and overall comfort and performance efficiency can also be predicted.

Although many questions remain unanswered as to the actual mechanisms of some types of insensible water loss, this does not in any way preclude their careful measurement and quantitation. An accumulation of data relating water losses to environmental changes will facilitate the development of a predictive equation to encompass these findings and may ultimately shed new light upon the mechanisms, themselves.

Having defined the influence of environment upon insensible water loss, fluid balance, and general comfort, one must next approach the question of physiologic regulation or adjustment of these functions. Does the state of hydration of the subject influence his rate of insensible water loss or his ability to adjust to a dry



environment? Do changes in peripheral blood flow or in fluid-electrolyte regulatory hormones have a measurable effect upon skin water losses?

These questions are particularly pertinent in light of the finding of significant variability in IWL<sub>5</sub> rates in the same subjects under identical environmental conditions. This variability was apparent despite the fact that all subjects were consistently in normal fluid balance.

Previous attempts to document changes in IWL rates directly related to alterations in fluid balance or peripheral circulation have not been generally successful, however (3, 53, 95). Most of these studies have depended upon local injection of materials together with local measurements of water loss rates. Some preliminary studies (92) have indicated that posterior pituitary extract can alter the rate of diffusion of water through excised dog skin as it does in frog skin (5), but these investigations must be extended to in vivo systems and to humans before any conclusions should be drawn.

Although subject-to-subject variations in insensible water loss rates can be satisfactorily explained on the basis of structural differences which alter permeability, a ready explanation for intra-subject variation is not now available (9, 86, 120, 130). When the role of physiologic changes within the subject in the determination of rates of IWL<sub>5</sub>, overall fluid balance, and sign-symptom development

has been defined, even more precise predictions of man's interaction with his environment can be achieved.

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TABLE I  
Classification of water losses from the human body

Sensible vs. insensible water losses	Common range of daily loss (gm.)
A. <u>Sensible</u> losses (liquid water)	1,100 to 7,600
Urine	1,000 to 2,000
Feces	100 to 500
Drooling and tearing	0 to 100
Vomitus	0 to 1,500
Significant thermal sweating (eccrine activity)	0 to 3,500
B. <u>Insensible</u> losses (vapor water)	600 to 2,650
Respiratory (expired air)	250 to 800
Light thermal sweating (eccrine activity)	0 to 400
Emotive (mental) sweating	100 to 500
Diffusional or nonsecretory skin losses	200 to 800
Metabolic gas exchange	50 to 150
C. Difficult to measure water losses	
Thermal sweating (over general body surface)( $W_T$ )	
Composed of sensible and insensible eccrine activity ( $W_{T_S} + W_{T_I}$ )	
Emotive or mental sweating (over palms, soles, axilla, forehead)--a secretory (eccrine and apocrine) type of water loss ( $W_M$ )	
Diffusional or nonsecretory skin loss (over general body surface)--a nonsecretory type of water loss ( $W_D$ )	
Respiratory loss (expired air brought close to 85% saturation with water vapor) ( $W_R$ )	
Metabolic gas exchange (not a true water loss, but represents the excess weight of carbon dioxide removed over the weight of oxygen absorbed during metabolism--it becomes important only for total-body gravimetric measurements) ( $W_G$ )	
Fluid balance equations:	
$W_Z = W_A + W_I - W_O - W_e + W_{O_2} - W_{CO_2}$	Basic Balance Equation
$W_{e_2} = W_A - W_Z + W_I - W_O + W_{O_2} - W_{CO_2}$	$W_{e_2}$ Indirect Skin IWL
$W_{e_2} = \text{Mean } W_e/\text{hr.} \times \text{duration (hr.)}$	$W_{e_1}$ Direct Skin IWL

TABLE II

## Previous measurements of skin insensible water losses

Investigator	Date	Technique	Site of measurement	Skin IWL rates* (gm./m. <sup>2</sup> /hr.)	In range of this study	Mean $\pm$ S. D. by techniques (gm./m. <sup>2</sup> /hr.)
THIS STUDY	1969	Whole body-gravimetric	---	6.00 - 15.00	---	---
Ikeuchi and Kuno (62)	1927	Whole body-gravimetric	---	10.51	Yes	10.97 $\pm$ 76
Wang et al. (122)	1930	Whole body-gravimetric	---	10.95	Yes	
Kerslake et al. (65)	1954	Whole body-gravimetric	---	12.40	Yes	
Brebner et al. (20)	1955	Whole body-gravimetric	---	10.80	Yes	
Thauer et al. (114)	1955	Whole body-gravimetric	---	9.50 - 12.50	Yes	
Hale et al. (56)	1958	Whole body-gravimetric	---	10.18	Yes	
Kuno (69)	1934	Dessic. capsule	Multiple	10.50	Yes	10.69 $\pm$ 2.20
Burch and Wilson (26)	1946	Dessic. capsule	Multiple	9.78	Yes	
Peiss and Hertzman (92)	1951	Dessic. capsule	Multiple	9.50	Yes	
Buettner (24)	1953	Dessic. capsule	Multiple	14.00	Yes	
Hertzman et al. (60)	1953	Dessic. capsule	Multiple	9.48	Yes	
Blank (17)	1952	Diff. chamber	Trunk	2.00	No	4.50 $\pm$ 3.50
Mali (73)	1956	Diff. chamber	Trunk	6.00 - 8.00	Yes	
Felsher and Rothman (41)	1945	CaCl bag	Abdomen	65.00	No	60.00 $\pm$ 7.00
Monash and Blank (83)	1958	CaCl chamber	Abdomen	20.00 - 90.00	No	
Rosenberg et al. (103)	1962	Electrohygrom.	Abdomen	1.50 - 2.40	No	5.33 $\pm$ 4.90
Spruit and Malten (107)	1965	Electrohygrom. -air flow	Forearm	5.00 - 17.00	Yes	
Baker and Kligman (3)	1967	Electrohygrom. -air flow	Trunk	2.00 - 4.00	No	
Goodman and Wolf (50)	1969	Infrared analysis-air flow	Forearm	5.40 - 8.40	Yes	---
Neuman et al. (86)	1941	Gravimetric-air flow	Multiple	20.00 - 80.00	No	30.30 $\pm$ 27.00
Pinson (95)	1942	Gravimetric-air flow	Trunk	6.00 - 12.00	Yes	
Burch and Winsor (27)	1944	Gravimetric-air flow	Abdomen	58.00	No	
Bettley and Grice (14)	1965	Gravimetric-air flow	Abdomen	3.50	No	

\* Average rate or range of rates at 760 mm Hg P<sub>B</sub>, 20 - 28° C. T<sub>a</sub>

TABLE III

Twenty channels of continuously monitored data (with subject  
on metabolic scale)

Measurement	Symbol	Number of channels	Sensitivity
Metabolic scale	$W_e$	1	$\pm 1.0$ gm.
Skin temperature	$T_{1..7}$	7	$\pm 0.1^0$ C.
Rectal temperature	$T_R$	1	$\pm 0.1^0$ C.
Black-globe temperature	$T_{BG}$	1	$\pm 0.2^0$ C.
Ambient temperature	$T_a$	2	$\pm 0.2^0$ C.
Water vapor pressure	$P_{H_2O}$	1	$\pm 0.5$ mm. Hg
Total pressure	$P_B$	1	$\pm 1.0$ mm. Hg
Partial pressure $N_2$	$P_{N_2}$	1	$\pm 1.0$ mm. Hg
Partial pressure $O_2$	$P_{O_2}$	1	$\pm 1.0$ mm. Hg
Partial pressure He	$P_{He}$	1	$\pm 1.0$ mm. Hg
Wind velocity	$V$	1	$\pm 20.0$ ft./min.
Heart rate	HR	1	$\pm 3.0$ b. p. m.
Respiratory rate	RR	1	$\pm 1.0$ b. p. m.



TABLE IV

General data on seven test subjects

Subject	Age	Ident.	Wt (kg.)	Ht (cm)	BSA (m. <sup>2</sup> )	VC (liters)	FEV (liters)	V <sub>E</sub> (liters/min.)	HCT	Hgb (gm.)	BUN	Creat (mg. %)	Na	K (mEq./liter)	Cl	CO <sub>2</sub>	T <sub>3</sub> (ug %)	T <sub>4</sub>
L B	19	B	74.65	185.9	1.98	5.48	4.30	9.2	47	15.5	12.5	1.2	147	4.5	103	26	29.3	7.8
W C	20	E	71.47	171.7	1.84	5.70	4.73	8.0	45	14.6	16.0	1.2	149	4.9	107	30	28.4	6.8
H D	19	A	72.42	183.4	1.94	6.02	4.62	7.8	46	14.8	16.0	1.4	145	4.2	105	29	28.9	7.1
K F	19	D, E	79.20	182.9	2.01	5.91	4.05	9.9	45	14.8	12.0	---	144	4.6	106	30	34.7	5.4
R H.	18	C	87.90	189.2	2.15	5.81	4.95	10.1	43	15.2	15.0	1.0	148	4.9	104	27	32.3	5.0
M K	18	F	77.77	186.7	2.03	6.02	4.84	8.7	46	15.1	16.0	1.2	150	4.7	104	30	32.9	6.3
P K	20	D(B, E)	61.94	169.5	1.72	4.40	3.65	6.7	48	16.2	22.0	1.4	149	4.8	105	28	36.1	4.1
Mean	19		75.05	181.3	1.95	5.62	4.59	8.6	45.7	15.2	15.6	1.2	147	4.7	105	29	31.8	6.7

TABLE V

Plan of insensible weight loss experiment

		Period	Control	E X P E R I M E N T A L				Control
		Part	1	2	3	4	5	6
		Duration	10 Days	21 Days	21 Days	13 Days	6 Days	10 Days
Environmental conditions	Symbol							
Total Pressure (mm. Hg)	$P_B$		700	700	258	258	480	700 565
Gas Composition	GC		77% N <sub>2</sub> (540 mm. Hg) 23% O <sub>2</sub> (160 mm. Hg)	77% N <sub>2</sub> 23% O <sub>2</sub>	30% N <sub>2</sub> (78 mm. Hg) 70% O <sub>2</sub> (180 mm. Hg)	100% O <sub>2</sub>  70% O <sub>2</sub> 30% He	67% N <sub>2</sub> 33% O <sub>2</sub>	77% N <sub>2</sub> 23% O <sub>2</sub>
Ambient temperature (°C.)	$T_a$		20 24 28	20 24 28	20 24 28	24	24	24 28
Water vapor pressure (mm. Hg)	$P_{H_2O}$		14	4 - 14	4 - 14	6.5 - 9	6.5 - 14	4 - 14
Air flow (ft./min.)	V		40	40 - 300	40 - 300	40	40	40

TABLE VI  
List of experiments

Experiment Ident	Duration (hr)	PB (mm Hg)	PH <sub>2</sub> O (mm Hg)	Ta (°C)	T <sub>ew</sub> (°C)	V (l/min)	G C	T <sub>S</sub> (°C)	W <sub>1</sub> (gm)	W <sub>0</sub> (gm)	W (gm)	VENT (liter/hr.)	WR (gm/m <sup>2</sup> /hr)	WR <sub>1</sub> (gm)	W <sub>e1</sub> (gm/m <sup>2</sup> /hr)	W <sub>e1t</sub> (gm)	W <sub>e2t</sub> (gm)	W <sub>e1t</sub> (gm)	-W <sub>e2t</sub> (gm/24 hr)	1WL <sub>1</sub> (gm/24 hr)	Number of Subjects	
1A	48	700	14.4	20.6	20.6	49	1	29.9	4536.2	3471.4	-162.1	535	3.1	297.6	5.9	561.6	853.4	-391.8	-195.9	10.4	496.8	6
1B	48	700	13.8	23.9	24.5	48	1	31.6	4704.7	3018.1	+44.5	532	5.1	489.6	6.7	642.4	1372.3	-729.9	-364.9	13.3	636.0	6
1C	48	700	14.5	27.9	28.3	41	1	33.8	5062.2	3023.2	+513.6	540	6.2	595.2	9.8	915.2	1260.5	-345.3	-172.7	17.5	835.2	6
2J	48	700	14.6	24.1	24.3	43	1	31.3	4717.3	3427.9	+81.2	538	4.5	432.0	6.4	510.4	938.5	-322.5	-161.2	12.4	592.8	6
2H	48	700	8.2	24.4	24.6	50	1	32.1	4690.7	2988.9	+260.6	538	5.9	566.4	7.9	725.6	1171.4	-445.8	-222.9	15.3	752.0	6
2G	48	700	6.5	24.5	24.9	54	1	32.1	4839.0	3750.1	-534.1	538	7.4	692.6	8.0	766.1	1353.4	-586.8	-293.4	16.9	836.4	6
2F	48	700	5.4	24.4	25.2	49	1	32.1	4799.3	3694.7	-123.1	538	8.0	748.8	8.9	821.6	955.9	-134.3	-67.2	18.4	874.4	6
2A	10	700	3.3	21.2	22.2	54	1	30.7				540	9.3	181.4	8.4					19.2	951.2	3
2C	10	700	9.0	20.1	21.6	54	1	30.3				480	8.8	171.6	8.4					18.7	898.8	3
2E	10	700	4.6	21.0	20.9	41	1	30.7				540	7.8	152.1	6.9					16.2	784.8	3
2P	10	700	14.2	28.2	29.2	49	1	33.3				480	6.6	128.7	9.1					17.2	744.0	3
2M	10	700	9.0	28.1	31.1	46	1	33.2				540	8.6	167.7	9.8					19.9	982.4	3
3J	48	258	13.9	23.4	27.0	46	2	32.0	4850.7	2823.1	+380.1	487	4.1	383.7	8.9	784.0	1376.8	-593.7	-296.9	14.5	674.4	6
3I	24	258	12.0	24.2	28.9	69	2	32.9	2133.3	1389.5	-36.9	487	4.7	219.9	9.5	440.4	645.9	-205.5	-205.5	15.7	752.0	6
3H	48	258	8.4	23.5	28.2	46	2	32.6	4862.3	2976.9	-242.1	487	5.6	524.2	10.2	896.0	1857.7	-961.7	-480.8	17.3	836.4	5
3G	48	258	6.1	23.7	27.3	45	2	32.8	5214.9	3028.4	+336.9	487	6.6	617.8	10.8	999.2	1579.9	-580.7	-290.4	18.9	920.8	6
3F	48	258	4.2	24.1	28.2	43	2	32.7	5114.0	3066.4	+234.5	487	7.3	683.3	11.7	1077.6	1543.4	-465.8	-232.9	20.8	1065.2	6
3A	10	258	4.3	20.7	25.7	45	2	30.8				513	7.8	152.1	9.1					18.4	982.8	3
3C	10	258	8.9	20.9	25.6	45	2	30.9				463	6.1	118.9	8.1					15.7	679.2	3
3E	10	258	14.2	20.9	26.0	46	2	31.5				513	3.0	58.5	6.4					10.9	528.0	3
3P	10	258	15.0	28.1	33.1	48	2	34.4				463	5.4	105.3	10.3					17.4	751.2	3
3M	10	258	9.1	28.6	32.5	46	2	34.0				513	7.8	152.1	11.2					19.0	921.6	3
3K	10	258	4.8	28.5	32.0	46	2	33.8				463	8.8	171.6	12.3					22.6	1046.8	3
4A	24	258	6.2	24.0	28.4	66	3	32.9	2073.3	1632.9	-258.7	466	7.2	336.9	11.2	518.8	564.3	-45.4	-45.4	19.9	936.4	6
4B	48	258	8.9	24.1	28.7	68	3	32.7	4997.8	3144.9	+191.4	466	5.0	468.0	10.4	964.8	1391.8	-427.0	-213.5	16.9	787.2	6
4C	24	258	6.3	24.2	29.8	82	4	32.1	2041.8	1730.2	-496.7	500	6.2	290.2	8.8	409.6	673.4	-263.8	-263.8	16.5	768.0	6
4D	48	258	8.9	24.3	28.8	63	4	32.4	4789.0	3105.3	+194.7	500	5.5	514.9	8.5	782.4	1237.2	-436.8	-218.4	15.5	722.4	3
5C	24	480	13.9	24.2	27.0	53	5	32.4	2081.7	1569.1	-183.5	493	3.4	159.1	7.5	345.6	561.2	-215.6	-215.6	12.4	578.4	6
5B	24	480	9.0	24.3	27.0	61	5	32.5	1956.7	1758.5	-282.9	493	4.5	210.6	8.4	389.2	346.2	+43.0	+43.0	14.4	669.6	6
5A	24	480	4.4	24.4	27.2	63	5	32.8	2034.5	1624.4	-309.6	493	7.3	341.6	9.8	458.4	587.9	-126.5	-126.5	18.6	866.4	6
6B	48	700	13.4	24.3	27.0	80	1	31.9	4592.5	3590.6	-263.1	510	4.5	421.2	7.3	670.4	995.2	-324.8	-162.4	13.3	619.2	6
6C	24	700	13.9	28.4	30.5	82	1	34.1	2316.7	1438.8	+122.9	514	5.6	262.1	9.9	460.4	622.2	-161.9	-169.9	17.0	792.0	6
6D	24	700	11.5	24.3	27.2	59	1	32.1	1878.3	1619.2	-479.6	512	3.9	182.5	7.5	345.6	603.1	-258.3	-258.3	12.9	600.0	6
7A	24	565	5.5	23.8	27.2	66	1	32.4	2003.3	1893.9	-587.8	530	7.8	365.1	9.3	444.2	562.4	-149.1	-149.1	18.9	887.2	6
2KQRS	24	700	7.0	28.1	31.7	61 -340	1	32.3	1780.0	1845.2	-671.4	488	7.1	332.3	11.2	513.6	471.2	+42.4	+42.4	19.8	931.2	4
2YTVW	24	700	9.2	28.4	32.5	52 -348	1	32.5	2105.0	1798.4	-398.0	488	6.1	285.5	12.4	555.0	565.2	+10.3	+10.3	20.0	854.4	4
3KQRS	24	258	6.8	28.2	31.1	47 -295	2	32.7	2205.8	1439.9	-324.7	445	5.9	276.1	12.8	570.0	937.8	-387.9	-387.9	20.2	950.5	4
3YTVW	24	258	9.2	28.2	31.4	47 -302	2	32.7	2350.0	1331.3	+79.2	445	6.3	294.8	12.2	547.2	806.8	-259.8	-259.8	19.9	852.0	4

# Key to TABLE VI

$P_B$	Range of $\pm 1$ mm. Hg
$P_{H_2O}$	Range of $\pm 0.5$ mm. Hg
$T_a$	Range of $\pm 0.5^\circ$ C.
$T_{ew}$	Range of $\pm 0.6^\circ$ C.
$V$	Range of $\pm 20$ ft./min.
GC	Gas Composition 1 = 21% $O_2$ , 79% $N_2$ 2 = 70% $O_2$ , 30% $N_2$ 3 = 100% $O_2$ 4 = 70% $O_2$ , 30% He 5 = 33% $O_2$ , 67% $N_2$
$T_s$	Range of $\pm 0.1^\circ$ C.
$W_I$	Total intake, liquids and solids
$W_O$	Total output, liquids and solids (exclusive of $W_{et}$ and $IWL_G$ )
$W$	Change in subject weight during experiment
VENT.	Pulmonary ventilation with subject on metabolic scale (expired volumes measured)
$W_R$	Respiratory insensible water loss (also $IWL_R$ )
$W_{Rt}$	Total $W_R$ for an experiment ( $W_R \times$ hours duration $\times$ B. S. A.)
$W_{el}$	Skin insensible weight loss ( $IWL_S$ ) measured directly on metabolic scale.
$W_{elt}$	Total $W_{el}$ for an experiment ( $W_{el} \times$ hours duration $\times$ B. S. A.)
$W_{e2t}$	Total $IWL_S$ for an experiment calculated indirectly using weight balance equation (Table I)
$W_{elt} - W_{e2t}$	Difference between $W_e$ ( $IWL_S$ ) calculated directly and calculated indirectly
$IWL_T$	Total insensible water loss ( $= IWL_S + IWL_R + IWL_G$ ), calculated from $W_{Rt} + W_{elt} + W_{Gt}^*$  * $W_{Gt} = W_{O_2} - W_{CO_2} \times$ hours

TABLE VII

Controlled diet during study (per 24-hour period)

	Carbohydrates (gm. )	Fats (gm. )	Protein (gm. )	Total kilocalories
Basic diet.	375	114	95	2,811
Diet of subject C	421	124	108	3,152

TABLE VIII

Subject weight changes during 12-week experimental period  
(all weights in grams)

Subject	Initial weight	Final weight	Weight change	Average weight	S. D.*	S. E.*
A	71,775.0	71,369.0	-406.0	71,838.7	319.8	106.6
B	75,933.5	75,596.8	-336.7	75,459.8	596.0	210.7
C	87,930.7	87,817.2	-113.5	87,732.5	337.8	119.4
D	61,586.0	61,413.5	-172.5	61,241.0	619.6	234.2
E	69,574.0	72,690.0	+3,116.0	71,665.6	1,176.4	392.1
F	77,067.1	76,036.6	-1,030.4	76,763.7	553.0	195.5
Mean			+519.5			

\* Subjects weighed at 7-day intervals during 12 weeks.

TABLE IX

Inspired gas volumes (liters/hr.) at representative ambient conditions

Exp. Ident.	P <sub>B</sub> (mm. Hg)	P <sub>H<sub>2</sub>O</sub> (mm. Hg)	T <sub>a</sub> (° C.)	G C.	S U B J E C T S							Mean (all subj.)	Mean -D'	Mean -D
					A	B	C	D*	D**	E	F			
1A	700	14.4	20.6	1	Inspired gas volumes (to nearest 10 liters/hr.)**									
					480	550	610	430	590	490	540	527	517	543
1B	700	13.8	23.9	1	490	560	600	440	590	480	550	530	520	545
1C	700	14.5	27.9	1	470	570	600	440	600	490	530	<u>529</u>	<u>514</u>	<u>540</u>
700 mm. Hg P <sub>B</sub> Experiments Mean												529	517	543
3J	258	13.9	23.4	2	440	510	570	400	560	450	510	491	480	506
3F	258	4.2	24.0	2	450	510	560	400	---	440	520	<u>480</u>	<u>480</u>	<u>496</u>
258 mm. Hg P <sub>B</sub> Experiments Mean												487	480	501
4A	258	6.2	24.0	3	420	510	550	410	---	430	500	470	470	482
4C	258	6.3	24.2	4	450	540	580	420	---	460	530	495	495	512
5C	480	13.9	24.2	5	460	530	560	430	---	460	510	491	491	504

\* Did not participate in all experiments.  
See table VI for key.

\*\* Corrected to ambient conditions

TABLE X  
Gas exchanges of subjects on metabolic scale

T <sub>a</sub> (° C.)		A	B	C	D	D'	E	F	Mean	Mean -D	Mean -D'
	B. S. A. (m. <sup>2</sup> )	1.94	1.98	2.15	1.72	2.01	1.84	2.03	1.95	1.99	1.94
24° C.	O <sub>2</sub> cons. (liters/hr.)	15.70	16.00	16.90	14.50	16.30	14.90	16.60			
	CO <sub>2</sub> prod. (liters/hr.)	12.90	13.10	13.90	12.20	13.50	12.70	14.00			
	O <sub>2</sub> - CO <sub>2</sub> (gm./hr.)	-2.96	-2.80	-3.07	-3.16	-3.13	-3.51	-3.63	-3.20	-3.20	-3.20
	R. Q.	.83	.82	.83	.84	.83	.85	.85	.84	.84	.84
20° C.	O <sub>2</sub> - CO <sub>2</sub> (gm./hr.)	-3.05	-2.98	-3.22	-3.28	-3.27	-3.69	-3.77	-3.30	-3.30	-3.30
28° C.	O <sub>2</sub> - CO <sub>2</sub> (gm./hr.)	-2.87	-2.75	-2.86	-3.10	-3.01	-3.40	-3.52	-3.10	-3.10	-3.10



TABLE XI

Estimated average gas exchange for 24-hour experiment  
(based on O<sub>2</sub> consumption of 25 liters/hr.)

T <sub>a</sub> (° C.)	R. Q.	O <sub>2</sub> - CO <sub>2</sub> (gm./hr.)	O <sub>2</sub> - CO <sub>2</sub> (gm./24 hr.)
20	.84	-5.41	-129.8
24	.84	-5.33	-127.9
28	.84	-5.25	-126.0

TABLE  
OBJECTIVE

XII  
EVALUATION

Area	1	2	3	4	5	
EYES	NORMAL	Mild tearing	Moderate tearing	Mild Redness	Mod-severe redness	
NOSE	NORMAL	Mild edema/redness	Mod-severe edema/red	Crusting/cracking	Bleeding	
LIPS	NORMAL	Slightly dry	Moderately dry	Cracking/peeling	Bleeding	
TONGUE	NORMAL	SI -Mod dry	Coated	Redness	Crusting/cracking	
MOUTH	NORMAL	Slightly dry	Moderately dry	Redness	Crusting/cracking	
PHARYNX	NORMAL	Slightly red	Mod. -severe redness	Cracking/edema	Exudate, bleeding	
SCALP	NORMAL	Mild scaling	Mod. -scaling	Severe scaling	Crusting/bristling	
SKIN	NORMAL	SI dry/scaling	Mod dry/scaling	Severe dry/scaling	Cracking/peeling	
GENERAL	NORMAL	Slightly ill	Moderately ill	Very ill	Request termination	
OTHER		List signs from 1 to 5 and describe				
	SUBJECTIVE		EVALUATION			
	1.	2	3	4	5	6
EYES	NORMAL	Slight burning	Mild burning	Mod-burning/pain	Severe burning/pain	Blurring vision/other
NOSE	NORMAL	Slightly stuffy	Mod dry/stuffy	Coryza	Post-nasal drip	Obstruction/other
LIPS	NORMAL	Slightly dry	Mod dry/chapped	Severely dry/chapped	Cracking	Painful/burning/other
TONGUE	NORMAL	Slightly dry	Moderately dry, burning	Very dry/burning	Painful/sev burning	Loss of taste/other
MOUTH	NORMAL	Slightly dry	Moderately dry/burning	Very dry/burning	Painful/sev burning	Swelling/other
PHARYNX	NORMAL	Slightly dry	Moderately dry/burning	Very dry/diff swallow	Painful/burning	Difficulty swallowing/other
SCALP	NORMAL	Mild itch	Moderate itch	Severe itch/burning	Severe burning	Tingling/other
SKIN	NORMAL	Slightly dry/itch	Moderate itch	Severely dry/itching	Cracking/painful	Burning/other
GENERAL	NORMAL	Slightly ill	Moderately ill	Very ill, uncomfortable	Request termination	-----
OTHER		List symptoms from 1. to 6 and describe				

TABLE XIII

Effects of increases in environmental variables on changes in rate of insensible water loss from the skin

Environmental Condition	Range	Change in rate of skin IWL			
		Qualifying Conditions	Mean	Range	Units
Ambient temperature ( $T_a$ )	20 <sup>0</sup> - 24 <sup>0</sup> C. 24 <sup>0</sup> - 28 <sup>0</sup> C. 20 <sup>0</sup> - 28 <sup>0</sup> C.	700 mm. Hg $P_B$ 700 mm. Hg $P_B$ 258 mm. Hg $P_B$	+ 0.27 + 0.72 + 0.45	+0.24 to +0.30 +0.66 to +0.81 +0.42 to +0.48	gm./m. <sup>2</sup> /hr./1 <sup>0</sup> C. $T_a$ Same Same
Water vapor pressure ( $P_{H_2O}$ )	4 - 14 mm. Hg	---	- 0.27	-0.25 to -0.31	gm./m. <sup>2</sup> /hr./1 mm Hg $P_{H_2O}$
Total pressure ( $P_B$ )	258 - 700 mm. Hg	---	- 0.58	-0.55 to -0.63	gm./m. <sup>2</sup> /hr./100 mm Hg $P_B$
Wind velocity (V)	50 - 300 ft./min.	O <sub>2</sub> :N <sub>2</sub> atmosph.	+ 0.70	+0.61 to +0.84	gm./m. <sup>2</sup> /hr./50 ft./min. V
Gas composition (GC)	70% O <sub>2</sub> :30% N <sub>2</sub> 100% O <sub>2</sub> 70% O <sub>2</sub> :30% He	258 mm. Hg $P_B$ 258 mm. Hg $P_B$ 258 mm. Hg $P_B$	0 + 2.00% -18.00%	N. A.	N. A.

TABLE XIV

Step-wise multiple regression analysis of the influence of physical factors  
upon the rates of skin insensible water loss

Physical factor	Cumulative correlation coefficient	F Value*	T Value*	P Value*
$T_{ew}$	1 0.530	214.7	14.65	.001
$P_{H_2O}$	1 → 2 0.591	146.6	- 7.52	.001
M. W. of gas	1 → 3 0.618	112.4	5.40	.001
$T_a$	1 → 4 0.636	91.43	4.34	.001
V	1 → 5 0.655	77.40	3.79	.005
$P_B$	1 → 6 0.684	59.94	- 2.72	.01

\* Noncumulative values

TABLE XV

Individual subject bias (deviation from grand mean value for all subjects  
in all experiments) in determinations of  $IWL_S$  and  $IWL_R$

Subject	Number of experiments considered	Deviation from grand mean value (gm./m. <sup>2</sup> /hr.)	
		$IWL_S$	$IWL_R$
A	26	-5.5%	-6.1%
B	26	+0.4%	+4.2%
C	26	+0.2%	+2.3%
D	20	+16.5%	+1.5%
D'	6	-5.6%	+7.7%
E	26	+3.3%	-3.8%
F	26	-14.3%	-5.1%

TABLE XVI

Variation in IWL<sub>S</sub> measurements in the same subject with ambient conditions held constant

Subject	Experiment 1-B			Experiment 3-G		
	Mean* (gm./m. <sup>2</sup> /hr.)	S. D. *	S. E. *	Mean* (gm./m. <sup>2</sup> /hr.)	S. D. *	S. E. *
A	5.4	0.76	0.38	10.4	1.40	0.70
B	7.6	1.41	0.72	10.9	0.66	0.33
C	7.6	0.32	0.16	10.6	0.72	0.36
D, D'	6.9	0.73	0.37	12.8	1.21	0.61
E	6.3	0.84	0.43	10.9	1.52	0.75
F	6.1	1.02	0.51	9.1	1.11	0.54

\* Forty-eight hour experiment; mean, S. D., and S. E. of four determinations of IWL<sub>S</sub> for each subject

TABLE XVII

Sign-symptom frequency-severity index values for experiments  $\geq$  24-hr. duration

PH <sub>2</sub> O (mm. Hg)	P <sub>B</sub> (mm. Hg)	Symptom index	Signs (by subject)	Signs (by physician)	Sign-symptom index
14	700	-0.64	-0.26	-0.09	-0.33
14	258	-0.74	-0.38	-0.05	-0.39
14	Mean	-0.69	-0.32	-0.07	-0.36
11.5	258	-0.70	-0.38	-0.25	-0.44
9	700	-0.64	-0.34	-0.24	-0.38
9	258	-0.71	-0.42	-0.27	-0.46
9	Mean	-0.67	-0.40	-0.25	-0.44
6.5	700	-0.68	-0.35	-0.21	-0.41
6.5	258	-0.88	-0.52	-0.33	-0.58
6.5	Mean	-0.78	-0.43	-0.27	-0.49
5	700	-1.12	-0.59	-0.35	-0.68
4	258	-1.21	-0.73	-0.45	-0.79
4.5	Mean	-1.18	-0.66	-0.40	-0.74
Overall range		-0.20 to -1.22	-0.11 to -0.73	+0.03 to -0.47	-0.18 to -0.83
Overall mean		-0.79	-0.44	-0.24	-0.49

TABLE XVIII

Sign and symptom frequency-severity rank

Area	Symptoms	
	Rank	Greatest frequency
Eyes	4	Slight burning
Nose	1	Slightly to moderately stuffy
Lips	2	Moderate chapping
Tongue	6	Slightly dry
Mouth	5	Slightly dry
Pharynx	3	Moderately dry
Scalp	7	Slight itch
Skin	8	Slight itch
General	9	Slightly ill
Signs		
Eyes	2	Mild to moderate tearing
Nose	3	Mild edema, redness
Lips	1	Moderately dry, cracking
Tongue	4	Dry; coated
Mouth	6	Dry, redness
Pharynx	5	Redness
Scalp	7	Moderate scaling
Skin	8	Slight scaling
General	9	Slightly ill



TABLE XIX  
Summary of specific sensory tests

Test	Experiments with significant change	T <sub>a</sub>	Ambient conditions P <sub>B</sub>	P <sub>H2O</sub>	GC*	Change	Sig. level (P)	Interpretation
Visual Acuity	2F	24.4	700	5.4	1	1.1	P < .01	Acuity significantly DECREASED
	3F	24.1	258	4.2	2	0.7	P < .05	Acuity significantly DECREASED
Schirmer Test	2F	24.4	700	5.4	1	- 6.0	P < .05	Tearing significantly DECREASED
	2YTVW	28.4	700	9.2	1	- 6.8	P < .05	Tearing significantly DECREASED
	3A	20.7	258	4.3	2	- 5.0	P < .05	Tearing significantly DECREASED
Gustometry	3F	24.1	258	4.2	2	-288.0	P < .01	Taste significantly DECREASED
	3H	23.5	258	8.4	2	- 60.0	P < .01	Taste significantly DECREASED
	3P	28.1	258	15.1	2	- 23.0	P < .05	Taste significantly DECREASED
	3M	28.6	258	9.1	2	- 21.0	P < .05	Taste significantly DECREASED
	4C	24.2	258	6.3	4	+ 33.0	P < .05	Taste significantly INCREASED
	4D	24.3	258	8.9	4	+ 53.0	P < .05	Taste significantly INCREASED
Olfactometry	3G	23.7	258	6.1	2	+ 5.2	P < .05	Smell significantly DECREASED
	3F	24.1	258	4.2	2	+ 4.2	P < .05	Smell significantly DECREASED

\* See table VI for key to GC  
Index numbers, no units

TABLE XX

Physical properties of gas mixtures, 300° K

Gas composition and %	Heat capacity (dimensionless)	Thermal conductivity (cal/cm-sec. °K x 10 <sup>6</sup> )	Viscosity (gm/cm-sec. x 10 <sup>6</sup> )
O <sub>2</sub> : N <sub>2</sub> 23 : 77 (air)	3.50	63.2	184.1
O <sub>2</sub> : N <sub>2</sub> 33 : 67	3.51	63.4	186.9
O <sub>2</sub> : N <sub>2</sub> 70 : 30	3.52	64.2	198.4
O <sub>2</sub> 100 -	3.53	64.8	207.1
O <sub>2</sub> : He      70 : 30	3.22	106.1	214.9

TABLE XXI

Effect of environmental parameters on total intake and output and their components  
(Significance levels are shown)

Measurement	Ambient conditions			
	$\uparrow P_B$	$\uparrow P_{H_2O}$	$\uparrow T_a$	$\Delta G.C.$
Total intake ( $W_I$ )	$\downarrow$ ( $<.05$ )	$\downarrow$ ( NS )	$\uparrow$ ( $<.05$ )	$\updownarrow$ ( NS )
Grand total output ( $W_O + W_{e_{lt}}$ )	$\uparrow$ ( $<.01$ )	$\downarrow$ ( $<.05$ )	$\downarrow$ ( $<.10$ )	$\updownarrow$ ( NS )
Respiratory insensible loss ( $IWL_R$ )	$\uparrow$ ( $<.05$ )	$\downarrow$ ( $<.01$ )	$\uparrow$ ( $<.02$ )	$\updownarrow$ ( NS )
Skin insensible loss ( $IWL_S$ )	$\downarrow$ ( $<.01$ )	$\downarrow$ ( $<.01$ )	$\uparrow$ ( $<.01$ )	** $\downarrow$ ( $<.05$ )
Total insensible loss ( $IWL_T$ )	$\downarrow$ ( $<.10$ )	$\downarrow$ ( $<.01$ )	$\uparrow$ ( $<.01$ )	** $\downarrow$ ( $<.05$ )
Weight change ( $W_Z - W_A$ )	$\downarrow$ ( NS )	$\updownarrow$ ( NS )	$\uparrow$ ( NS )	$\updownarrow$ ( NS )

\*  $\uparrow$  indicates an increase,  $\downarrow$  a decrease, and  $\updownarrow$  no change

\*\* He compared with  $O_2$  and  $N_2$

Fig. 1 Relationships of Difficult-to-Measure Water Losses. (See table I for symbol explanation). The horizontal dimensions are roughly proportional to the magnitude of each type of loss while the vertical dimensions have no importance.  $IWL_T$  (1) is composed of components 2, 7, and 3. As measured in this study,  $W_e$  (5) includes  $W_M$  and  $W_D$  since  $W_{T_i}$  (4) is absent. The three sources of weight loss actually measured on the metabolic scale when  $W_R$  (3) is trapped are denoted by 6. In practice  $W_e$  or  $IWL_S$  is determined by subtracting 3 and 7 from the total rate of weight change on the metabolic scale.

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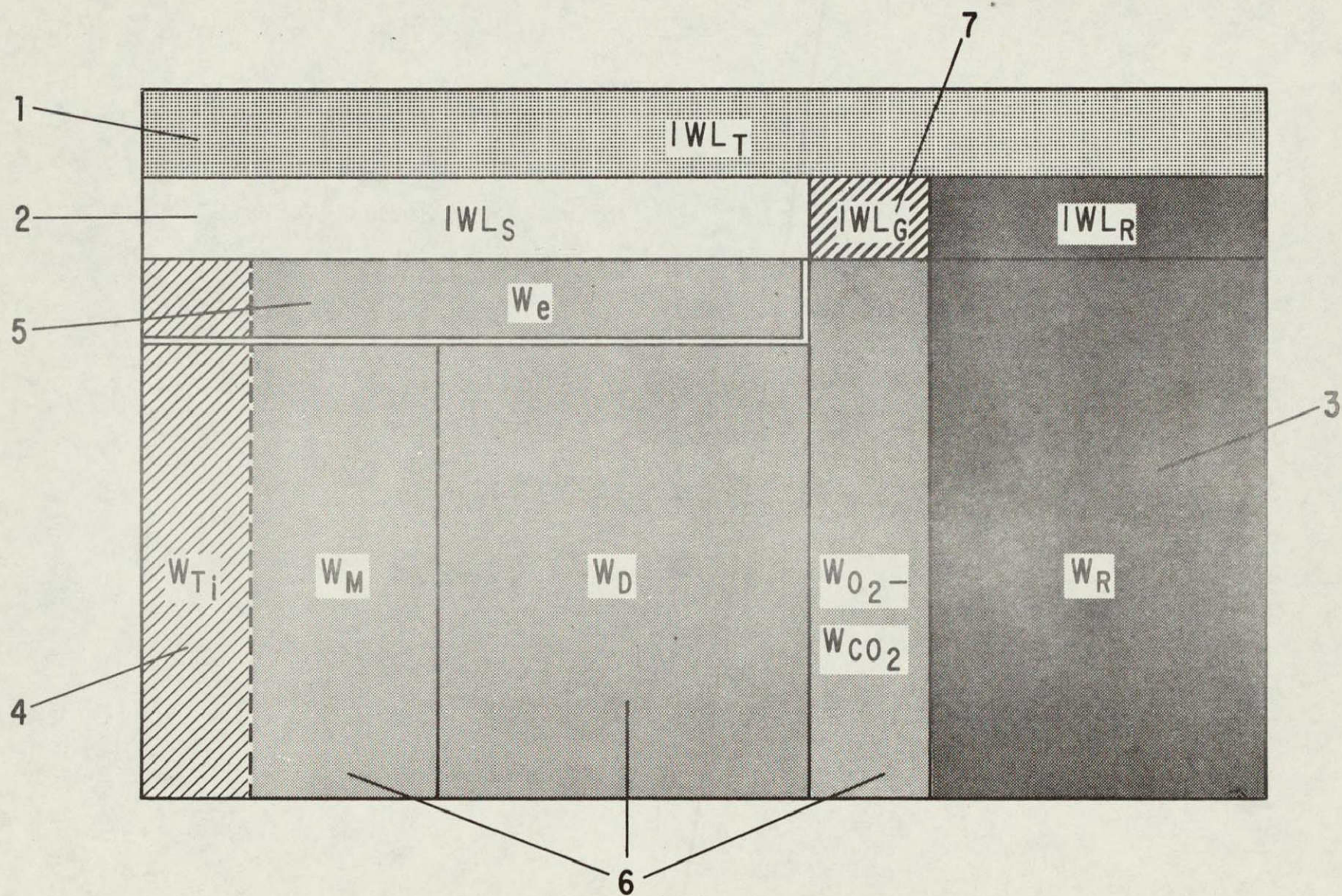
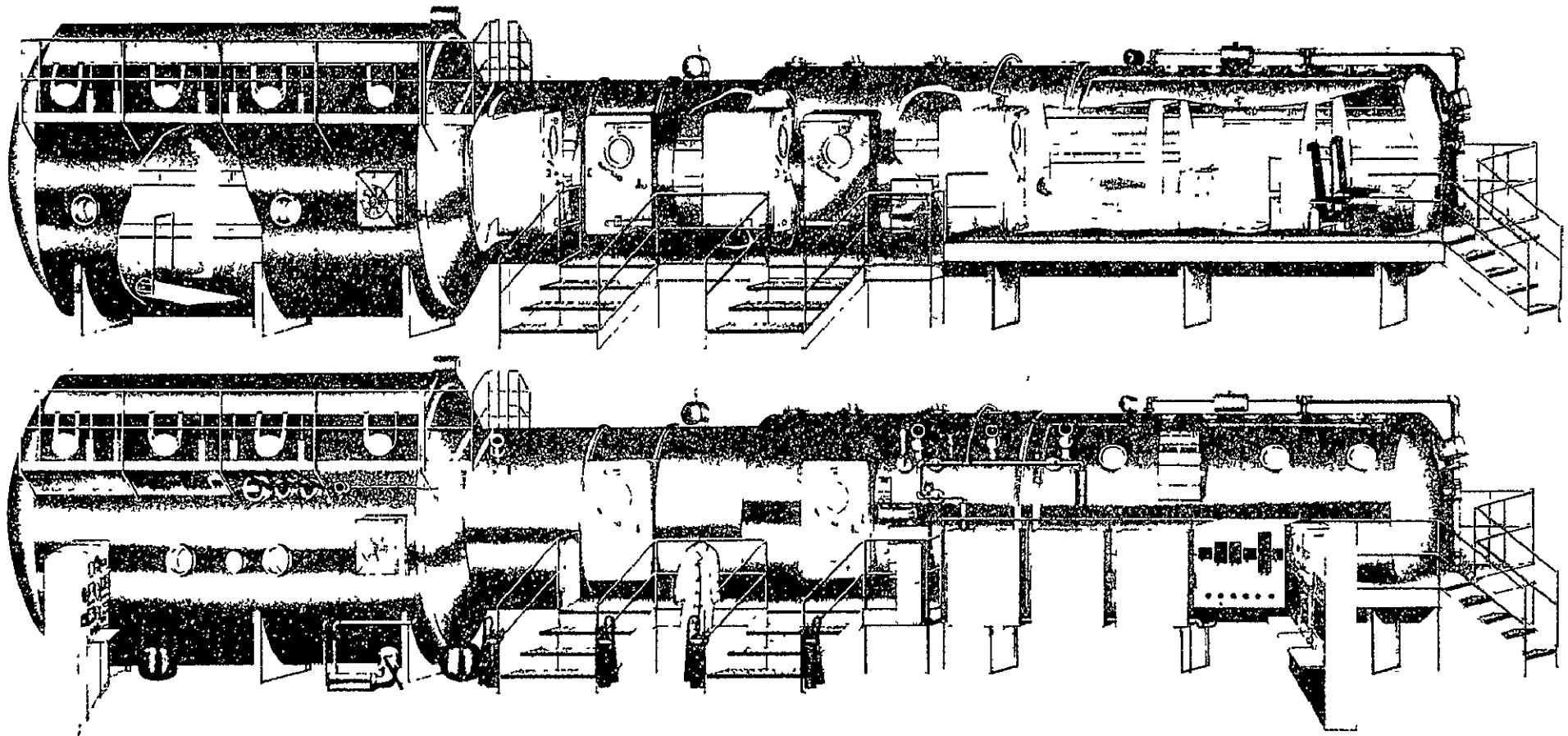


Fig. 2    Controlled Environmental Complex used in the study. Measurements of insensible water loss rates were conducted only in the laboratory section at left, while sleeping and eating were confined to the test cell at right.



# CONTROLLED ENVIRONMENTAL COMPLEX



## MISSION OBJECTIVES

- INVESTIGATE AND ESTABLISH PHYSIOLOGICAL LIMITS FOR MANNED ENVIRONMENTS APPLICABLE TO AIR FORCE REQUIREMENTS, E. G. AIRCRAFT AND SPACE CABIN ATMOSPHERES, AND MISSILE OPERATIONS
- FURTHER THE KNOWLEDGE BASE OF AEROSPACE PHYSIOLOGY THROUGH APPLIED RESEARCH.
- DETECT AND EVALUATE TRACE CONTAMINANTS GENERATED BY MAN WITHIN SEALED ENVIRONMENTS.
- OPERATE, MAINTAIN AND UPGRADE HYPOBARIC CHAMBERS AND ENVIRONMENTAL SIMULATORS TO PROVIDE A SAFE ATMOSPHERE FOR AEROSPACE RESEARCH

## CAPABILITIES AND CHARACTERISTICS

- OVERALL CONFIGURATION
  - FOUR MAN TEST CELL (LIVING AREA) 950 CUBIC FEET.
  - LABORATORY: 2000 CUBIC FEET
  - SYSTEM OF AIRLOCKS AND PASSLOCKS FOR TRANSFERRING OF SUBJECTS OR EQUIPMENT
- ATMOSPHERIC CAPABILITIES
  - ALTITUDES- GROUND LEVEL TO 34 THOUSAND FEET
  - TEMPERATURE- 35°- 85° F
  - HUMIDITY- 5% to 100% WATER PRESSURE TO 100% RELATIVE HUMIDITY.
  - ATMOSPHERE- ANY GASEOUS MIXTURE OF  $O_2$ ,  $CO_2$ ,  $N_2$ ,  $H_2$ , AND  $CO$  WITH 100%  $O_2$  CAPABILITY.  $O_2$ ,  $CO_2$  AND  $N_2$  ARE AUTOMATICALLY CONTROLLED
  - LIGHTING- DARK TO READING INTENSITY.
  - DATA- 32 CHANNELS OF DIGITAL TELEMTRY UNITS

## SAFETY FEATURES

- FIRE SUPPRESSION SYSTEM WITH AUTOMATIC UV DETECTION WITHIN 200 MILLISECONDS OR MANUAL ACTIVATION. FULL WATER FLOW OF 75 GALLONS PER MINUTE PER SQUARE FOOT WITHIN 700 MILLISECONDS OF DETECTION
- SMOKE, OVERHEAT AND ELECTRICAL FAULT DETECTION RAPID RECOMPRESSION FROM 34 THOUSAND FEET TO GROUND LEVEL IN 24 SECONDS.
- ALL INTERNAL EQUIPMENT AND MATERIALS NON-COMBUSTIBLE
- EMERGENCY POWER FOR LIGHTING AND COMMUNICATIONS

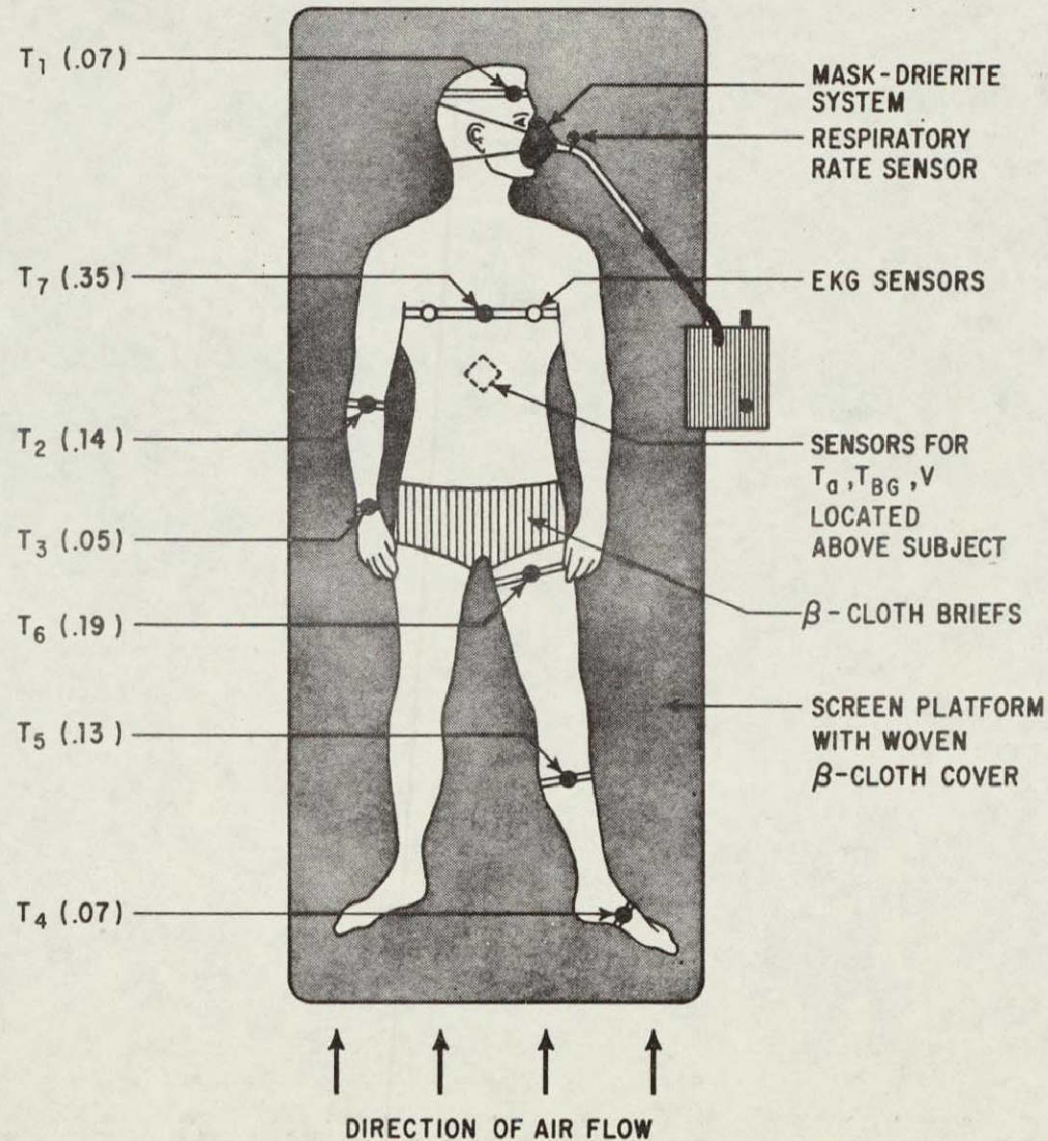
## EXPERIMENTAL CAPABILITIES

- LABORATORY- ADDITIONAL MEASUREMENT EQUIPMENT AS REQUIRED BY THE EXPERIMENTAL PROTOCOL.
  - TREADMILL
  - ERGOMETER
  - METABOLIC SCALE
  - WIND TUNNEL
  - REBREATHING SYSTEM

Fig. 3    Sensor and equipment positions for measurement of the skin and respiratory components of insensible water loss. Proportionality constants for determination of the weighted average skin temperature ( $T_s$ ) are shown.



# SKIN TEMPERATURE SENSORS AND PROPORTIONALITY CONSTANTS



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Fig. 4 Plan of typical 24-hr. experiment. Measurements of  $IWL_S$  and  $IWL_R$  were repeated three times at approximately eight-hour intervals on the metabolic scale ("2" on plan). Two rehydrated meals and two sleep periods ("12" and "11") were included.

# 24 HOUR EXPERIMENT

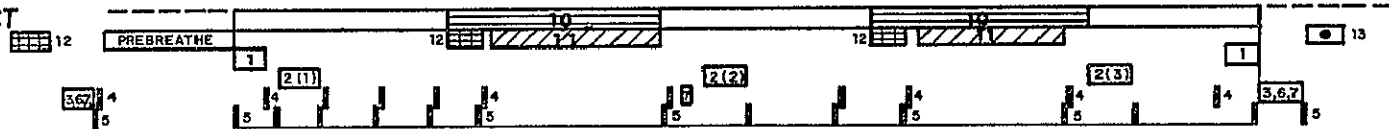
TIME 0700 0900 1100 1300 1500 1700 1900 2100 2300 0100 0300 0500 0700 0900 1100 1300 1500 1700 1900  
 -4 -2 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32

## LEGEND

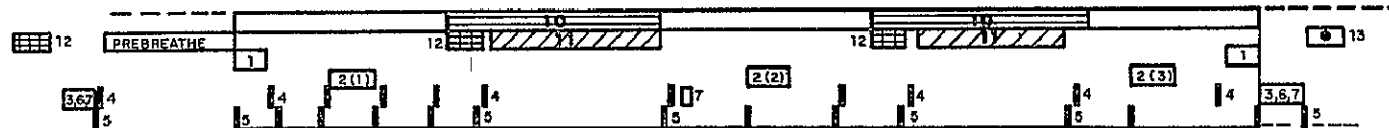
SYMBOL	TIME ALLOWED	KEY EVENT
	45"	TIME IN FOUR MAN CHAMBER
	45"	SLEEP
	45"	REHYDRATED MEAL NORMAL MEAL (BOX LUNCH)
1	15"	TOTAL BODY WEIGHT
2	60"	EVAPORATIVE WATER LOSS
3	15"	PHYSICIAN MED EVAL
4	4"	SUBJECT OBJ EVAL
5	2"	SUBJECT SUBJ EVAL
6	5"	GUSTOMETRY OLFACTOMETRY
7	10"	SHIRNER TEST VISUAL ACUITY

SUBJECT

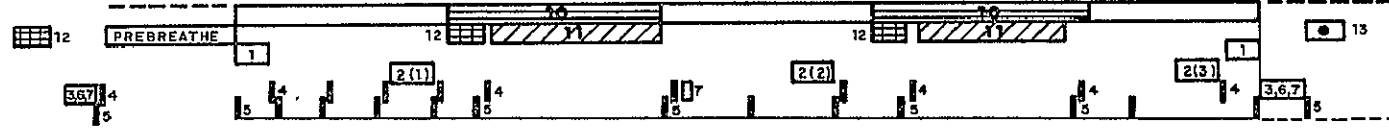
A



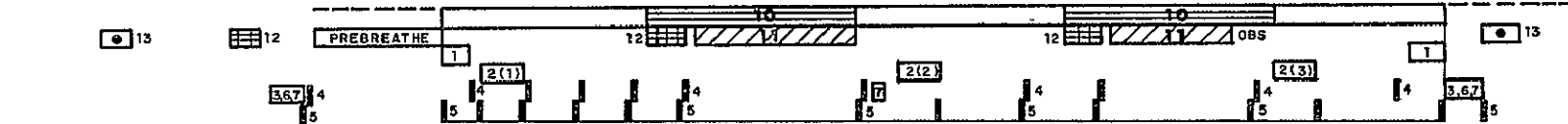
B



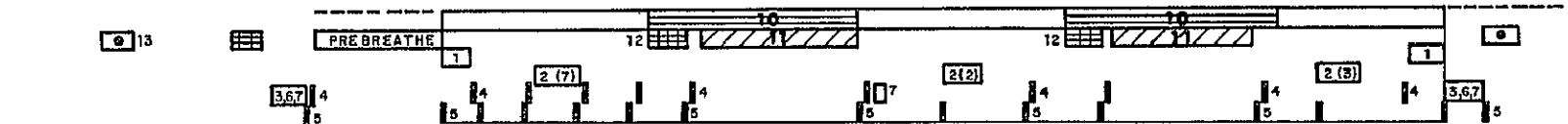
C



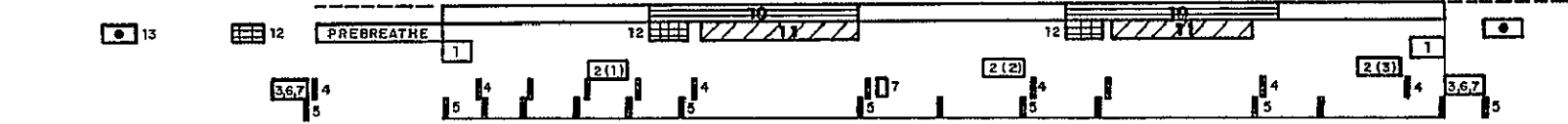
D



E



F



4-MAN  
OBSERVER \*1

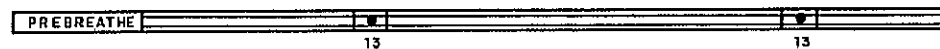


Fig. 5 Relationship of skin insensible weight loss to total barometric pressure ( $P_B$ ) and water vapor pressure ( $P_{H_2O}$ ) at  $24^{\circ}$  C.  $T_a$  and V below 100 ft/min. Pressures are expressed in mm. Hg. Significance levels for pressure differences are shown.

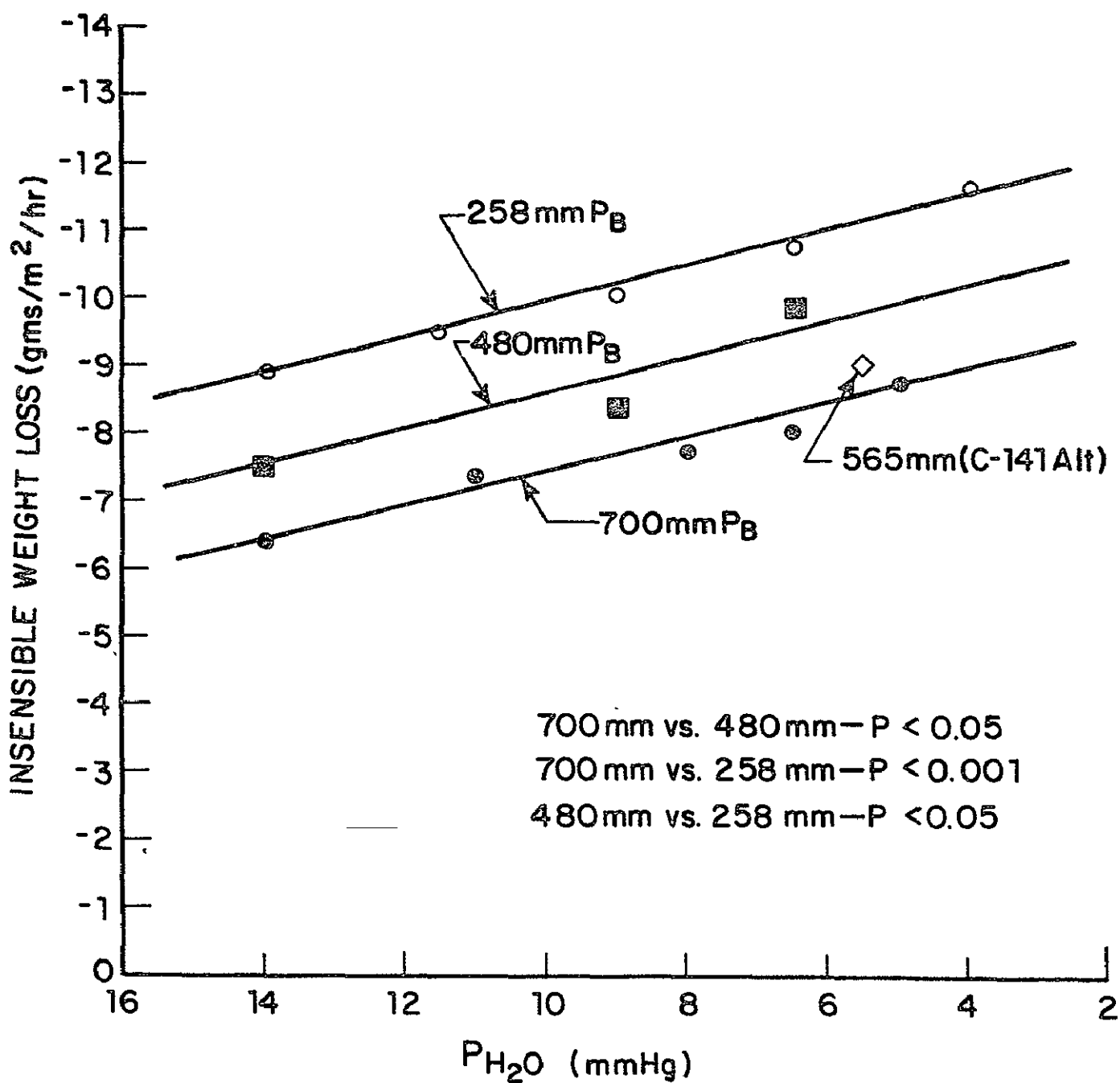


Fig. 6 Mean and standard deviations of skin insensible weight loss values collected on six subjects at two levels of  $P_B$  and five levels of  $P_{H_2O}$ . (Compare with Fig. 5).

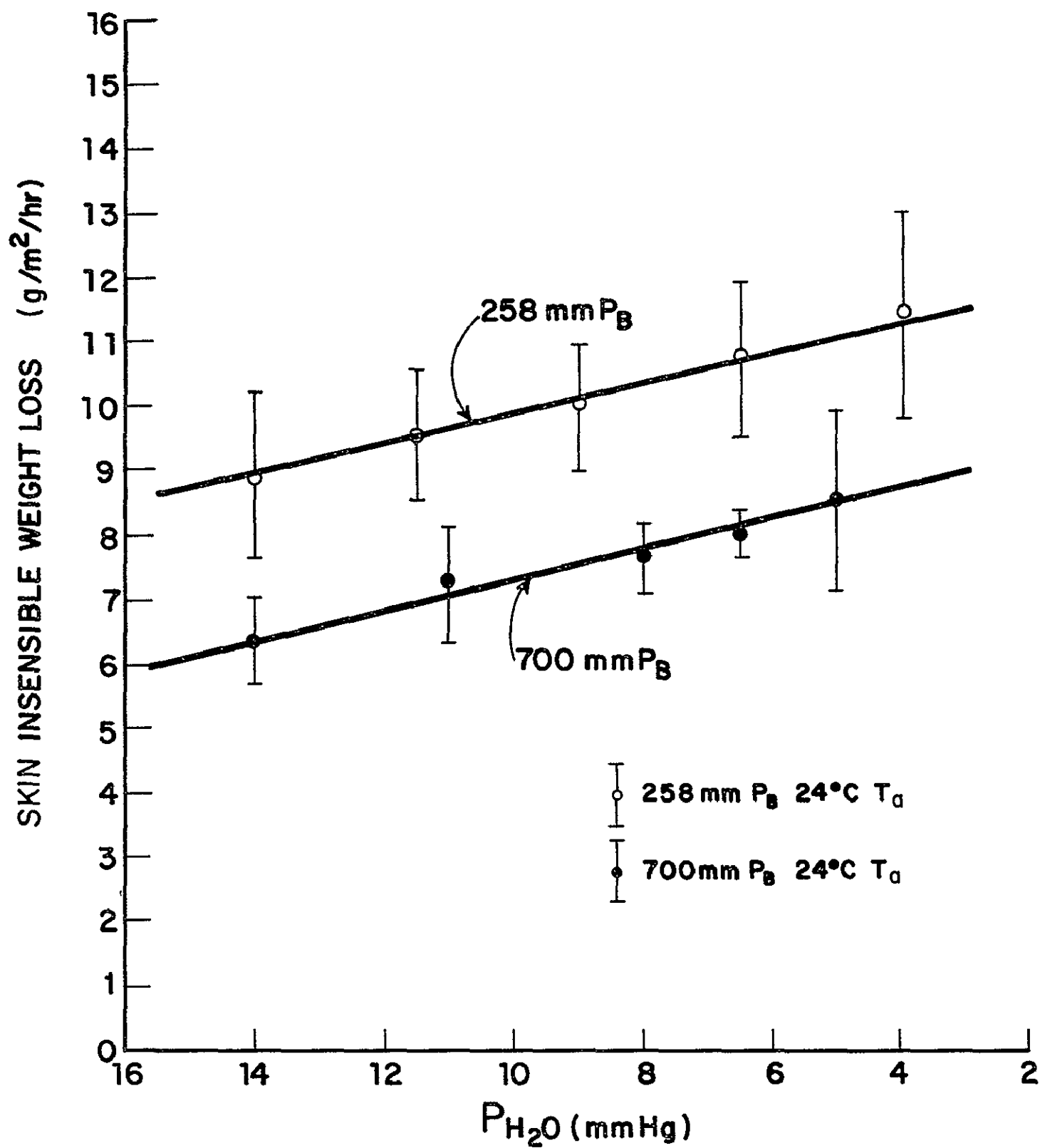


Fig. 7    Total range and mean of skin insensible weight loss values collected on six subjects at two levels of  $P_B$  and five levels of  $P_{H_2O}$ . (Compare with Fig. 5).



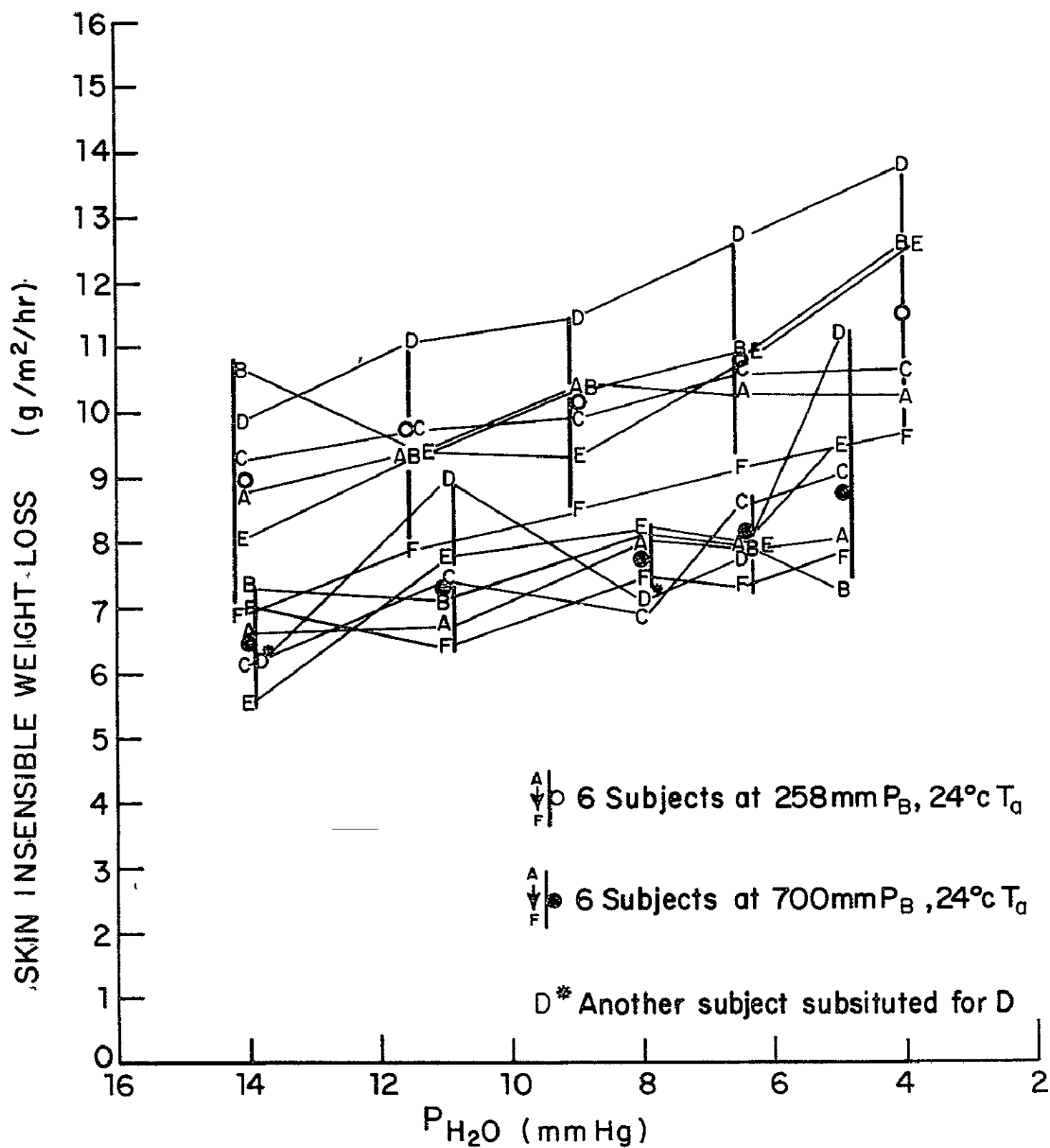


Fig 8. Relationship of atmospheric gas composition to skin insensible weight loss rates at 258 mm. Hg  $P_B$ , 24° C.  $T_a$ . Note the marked decrease in rate of water loss when He is substituted for  $N_2$ . Significance levels are shown.

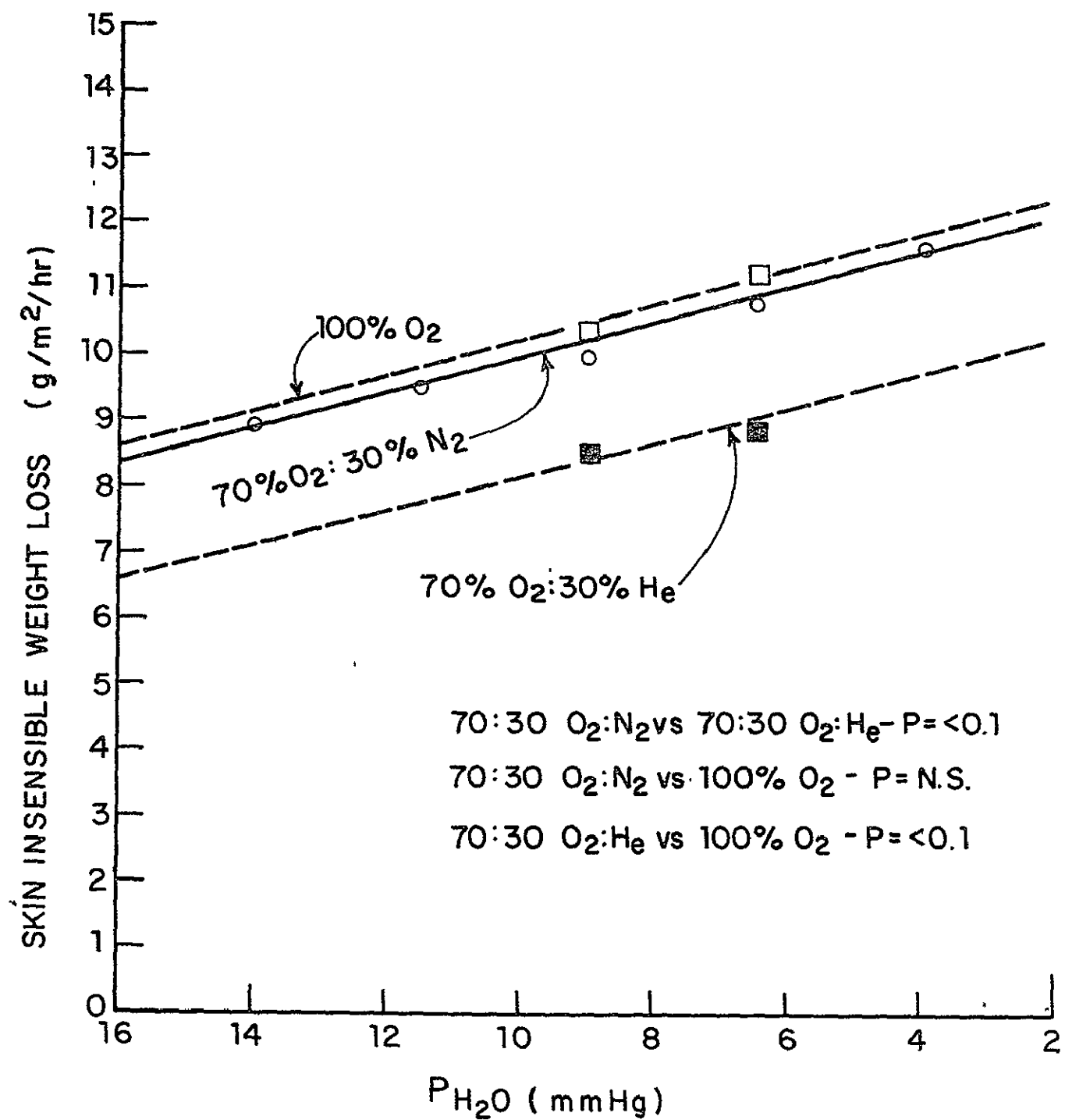


Fig. 9 Relationship of ambient temperature ( $T_a$ ) to rates of skin insensible weight loss at varying  $P_B$  and  $P_{H_2O}$ . Note the significant effect of  $P_B$  with a non-linear relationship occurring at 700 mm. Hg  $P_B$ . Significance values are also shown.

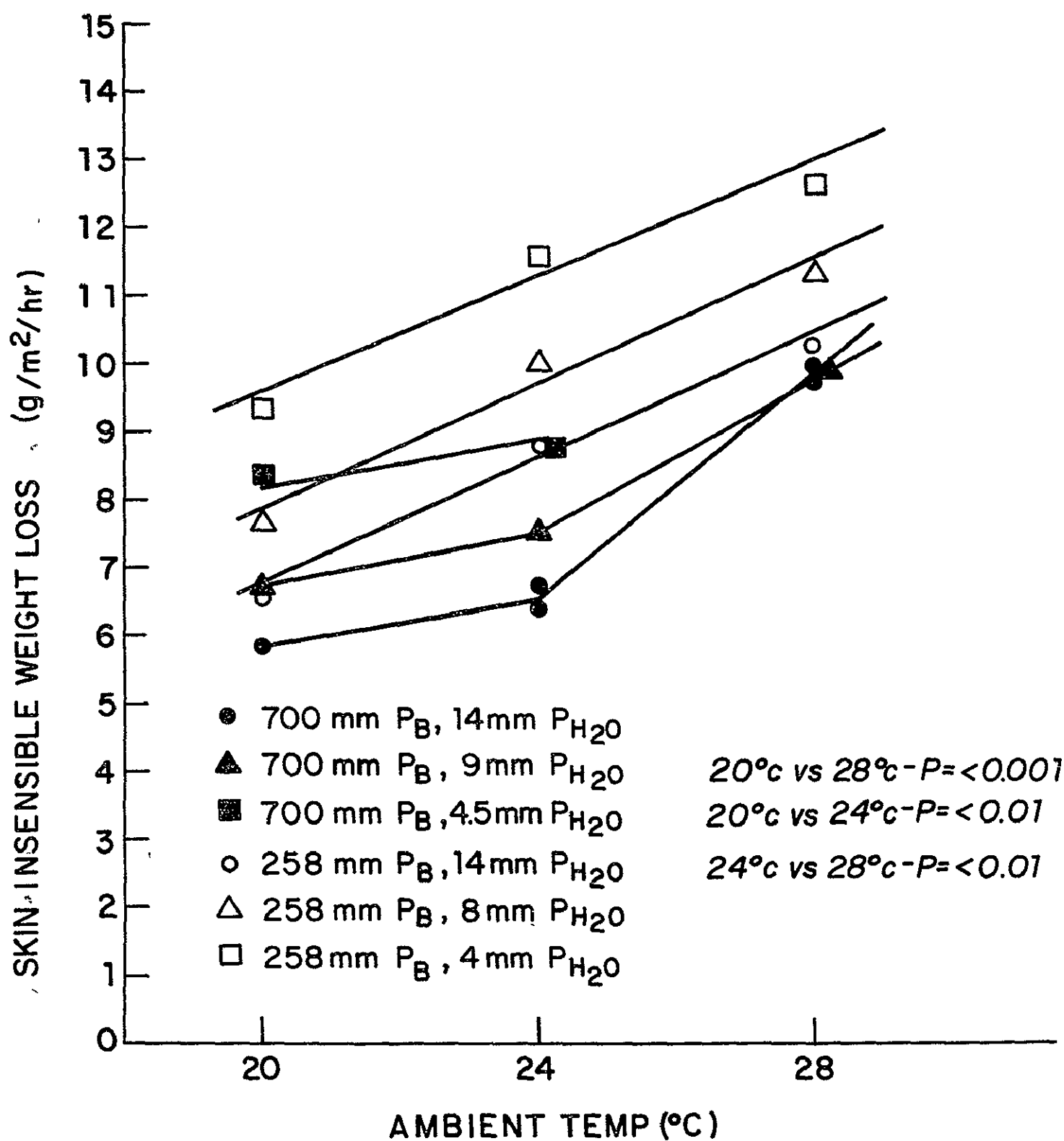


Fig 10 Mean and standard deviations for skin insensible weight loss rates in subjects exposed to varying  $T_a$ ,  $P_{H_2O}$ , and  $P_B$ . The interaction of total pressure with ambient temperature in altering the rate of change of IWLs with changes in  $T_a$  can be seen.

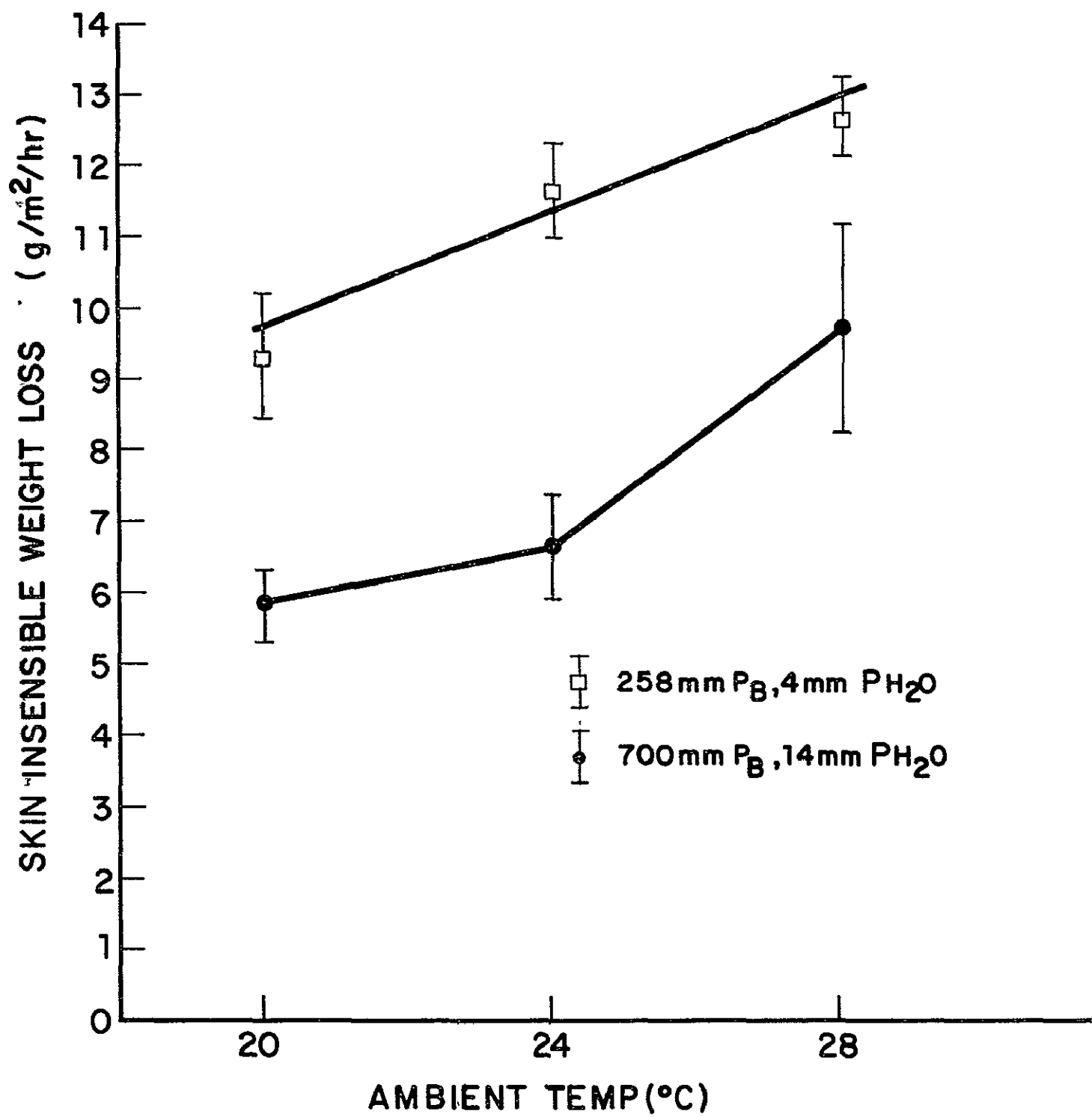


Fig. 11    Interaction of  $P_B$  and  $T_a$  with  $P_{H_2O}$  in determining rates of skin insensible weight loss. The iso- $P_B=T_a$  weight loss slopes are nearly parallel except for the 700 mm.  $P_B=28^\circ C. T_a$  line. Under these conditions, thermal sweating was noted at 14 mm. Hg  $P_{H_2O}$  causing a marked shift in the slope. Significance levels for the differences in IWL<sub>s</sub> rates with varying ambient conditions are shown.



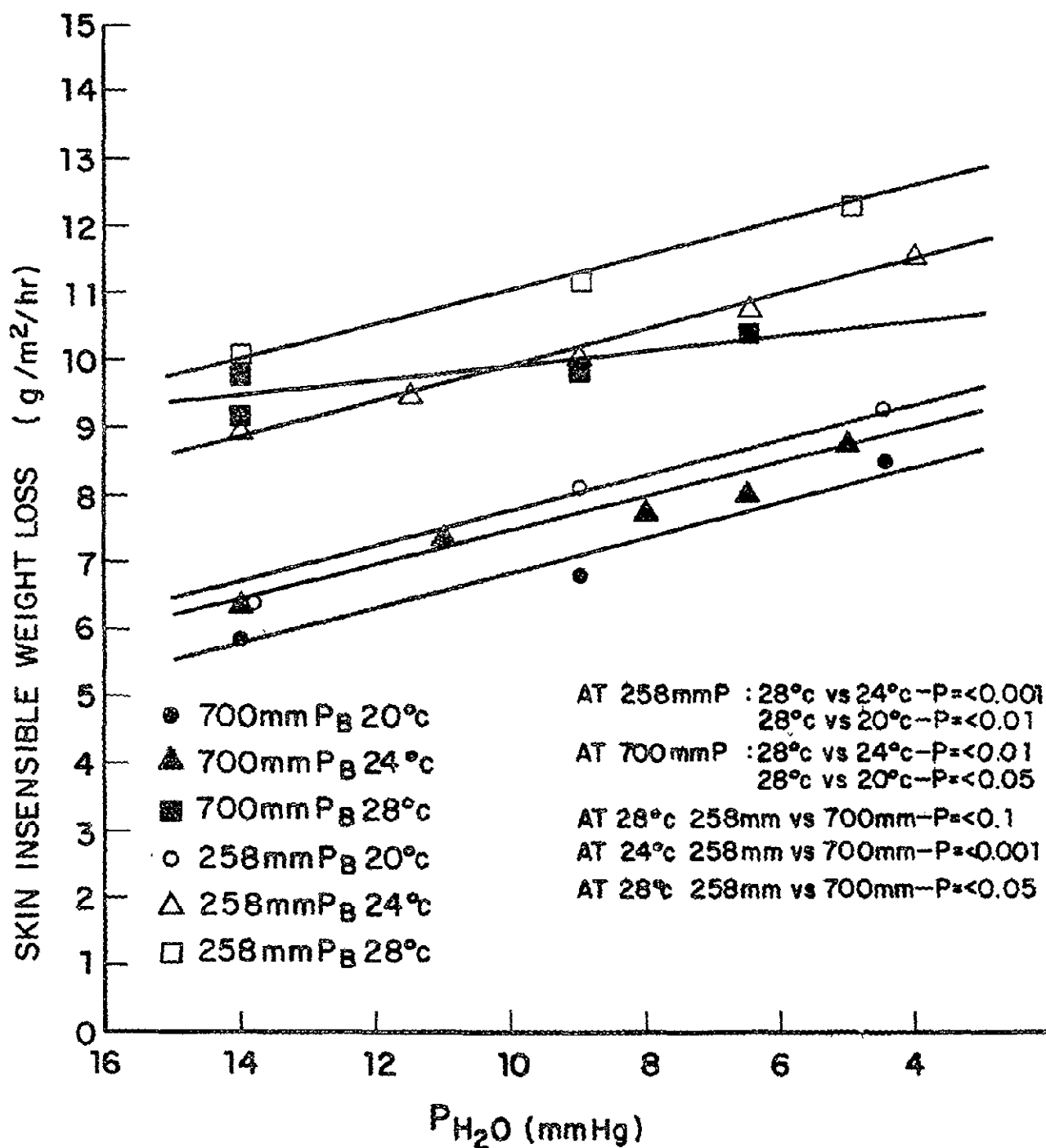


Fig. 12 Relationship of wind velocity ( $V$ ) to rate of skin insensible weight at  $28^{\circ}\text{C}$ .  $T_a$  and varying  $P_B$  and  $P_{H_2O}$ .  $V$  is expressed in both ft./min. and m./min. In the region of free convective cooling, the differences among the four values of  $IWL_s$  are significant to the .05 level. In the region of forced convective cooling, however, the value differences lose all significance.

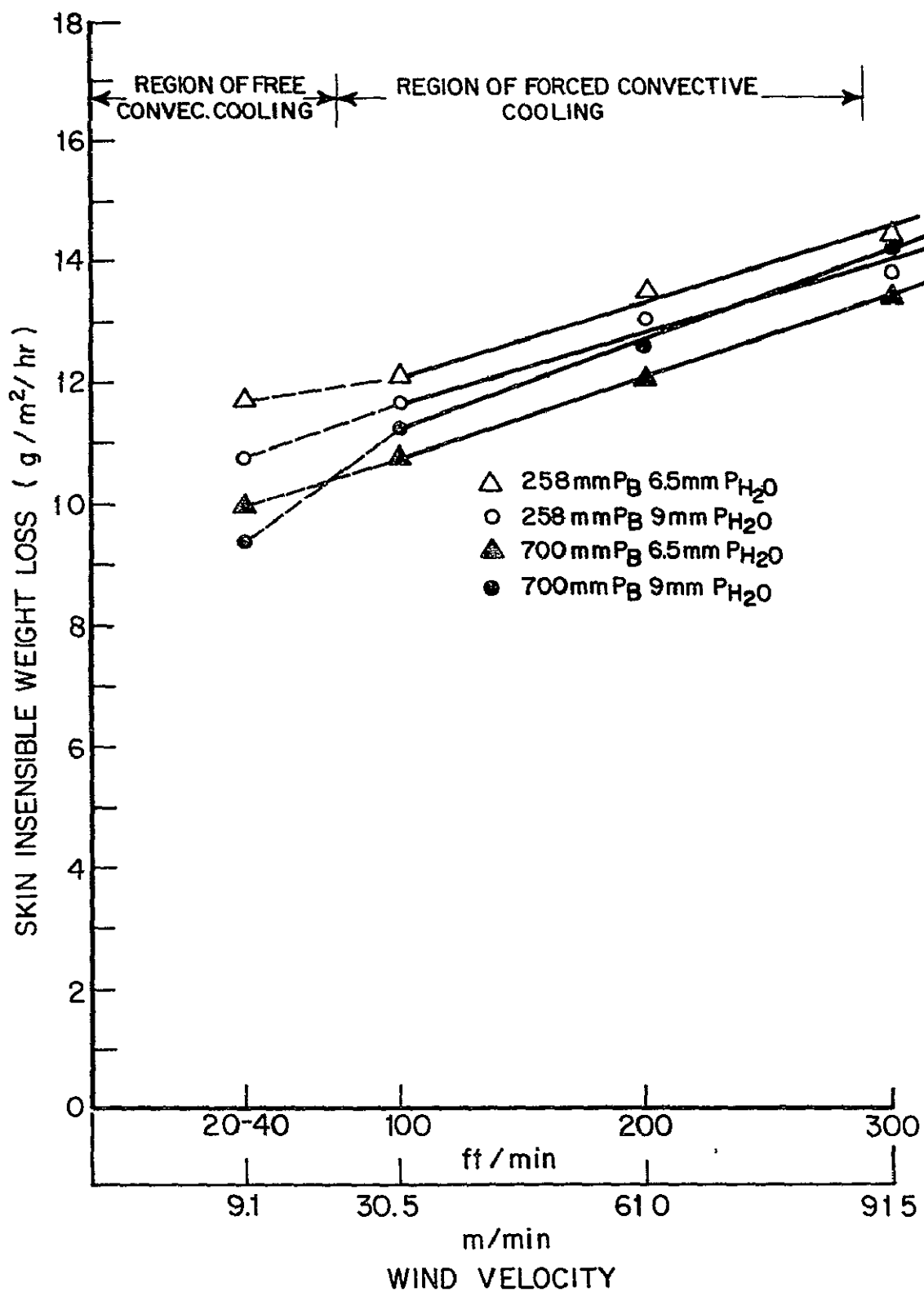


Fig. 13    Effects of increases in four environmental variables upon alterations in the rate of skin insensible weight loss. (The rates of change of IWL<sub>S</sub> are expressed in terms of units of environmental change.)

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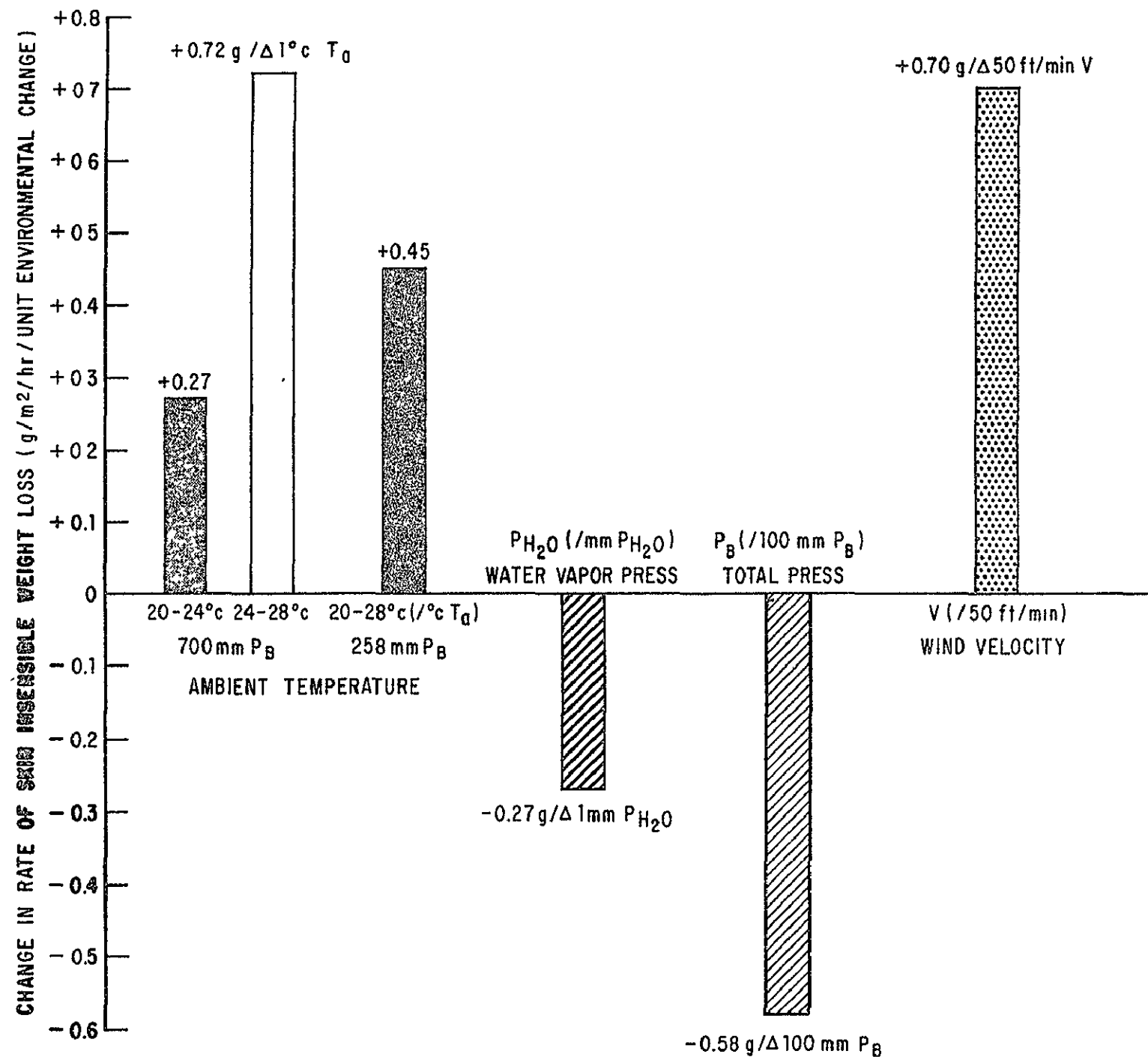


Fig. 14 Relationship of average skin temperature ( $T_s$ ) to  $T_a$  for varying combinations of  $P_B$ , G.C., and V. Note that  $T_s$  is consistently higher for a given  $T_a$  when the total pressure is reduced.

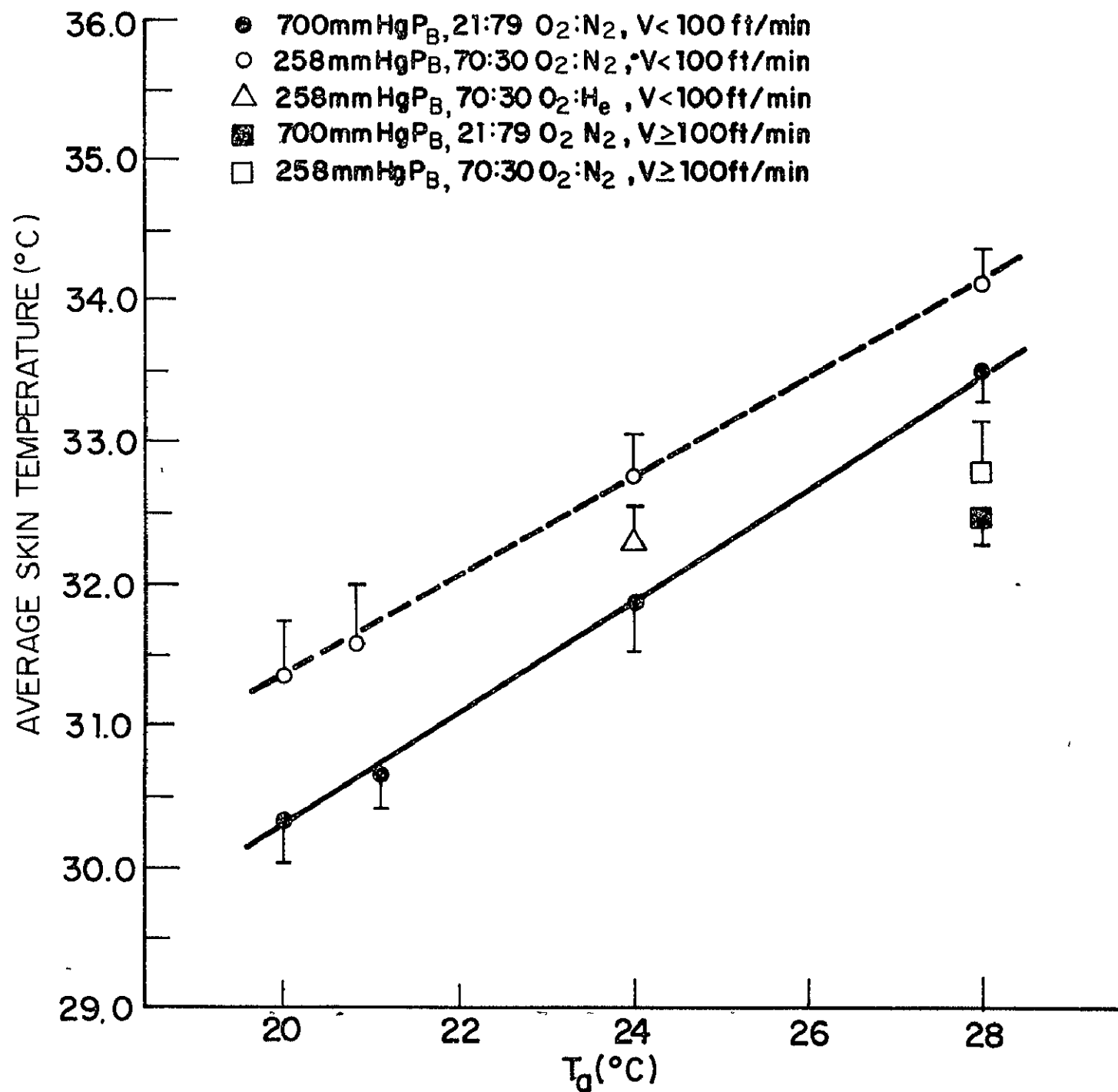


Fig. 15 Relationship of average skin temperature ( $T_s$ ) to skin insensible weight loss. A clear trend but a wide scatter is present. Note the marked effect of elevated wind velocities.



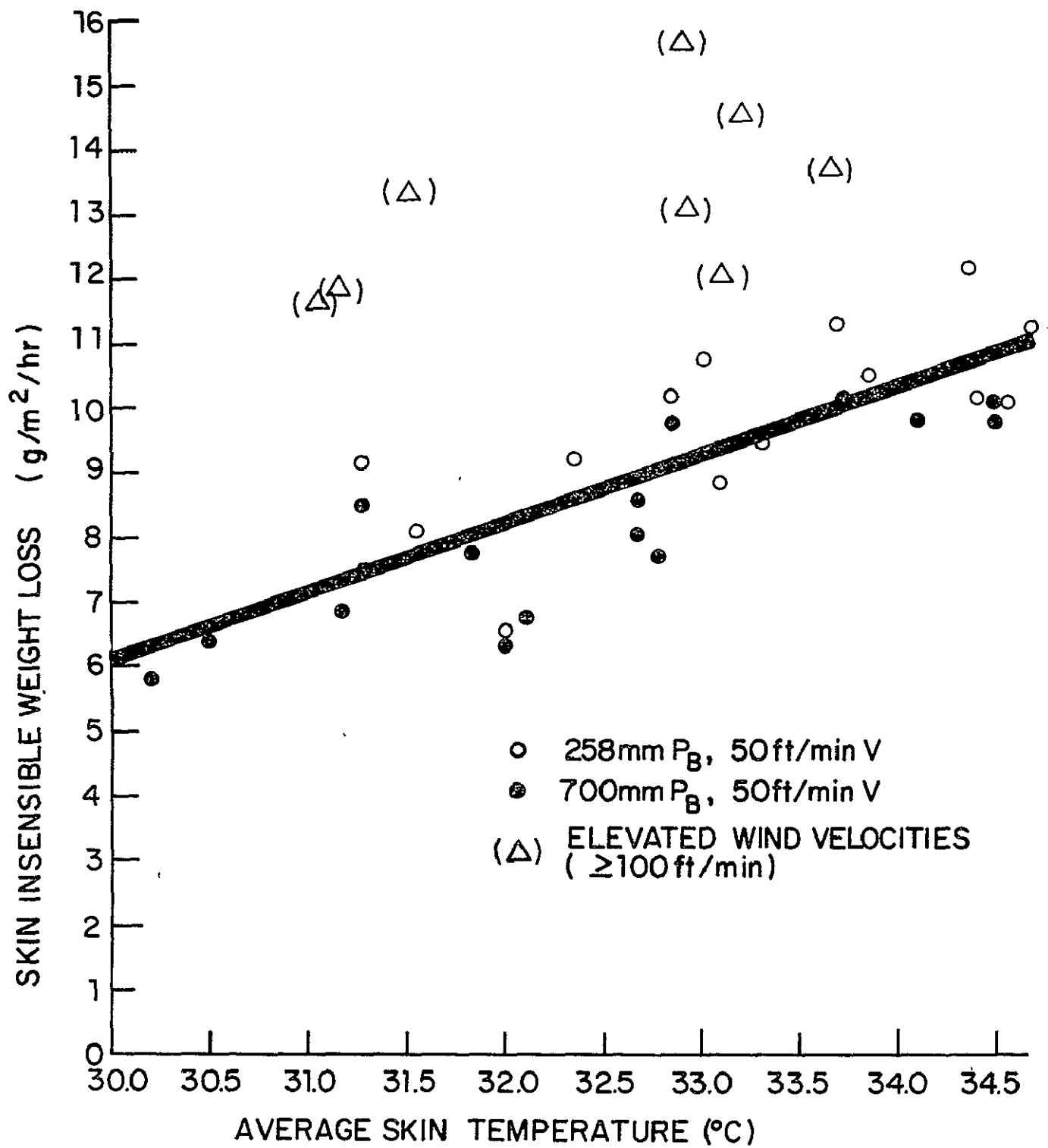


Fig. 16    Intake and output of six subjects during seven consecutive experiments at 700 mm. Hg  $P_{B_1}$ . Grand total output includes all sources of weight loss except  $IWL_G$ .

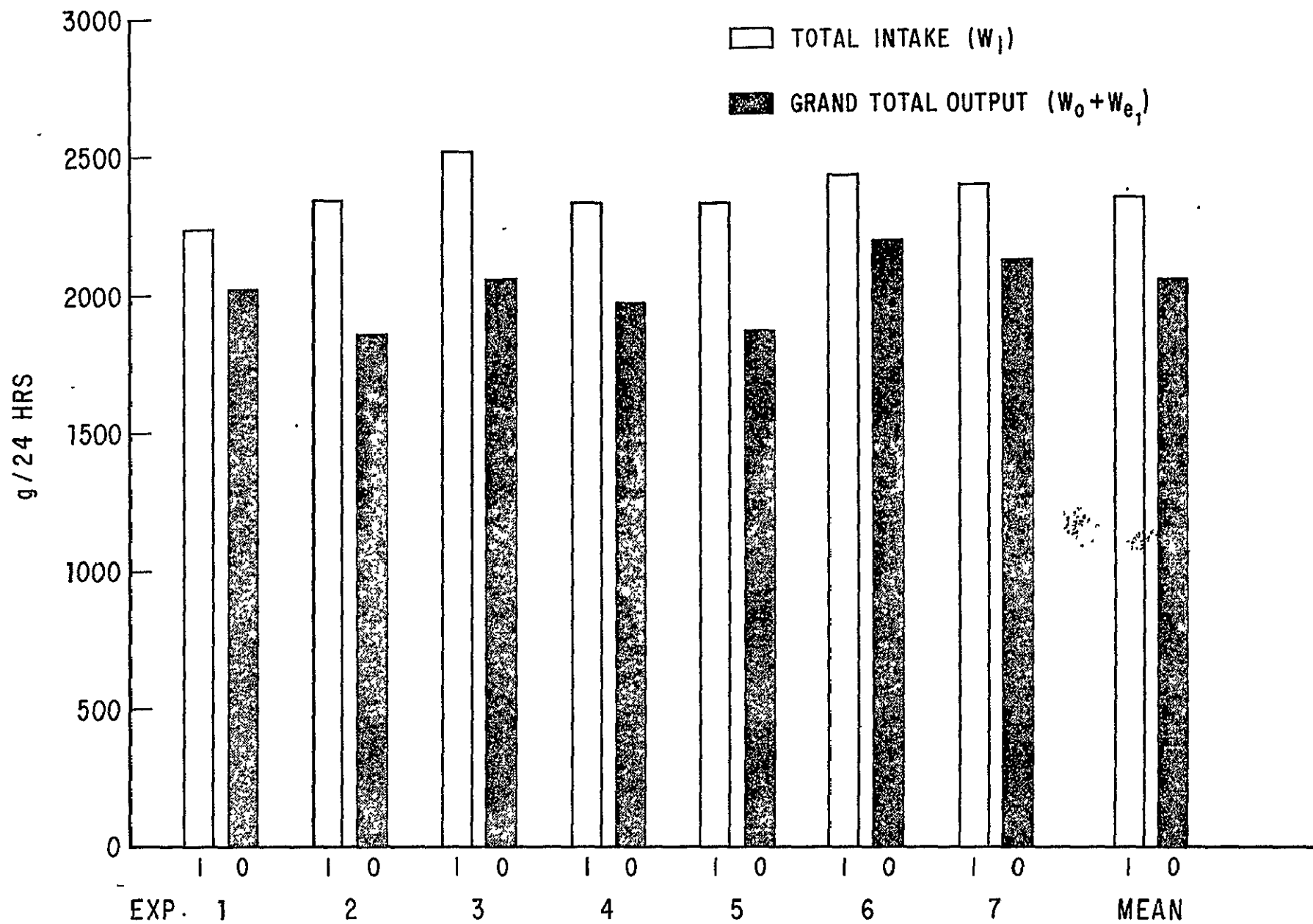


Fig. 17 Effect of total barometric pressure ( $P_B$ ) upon weight balance and fluid loss (paired 48-hr. and 24-hr experiments). Significance levels are shown.

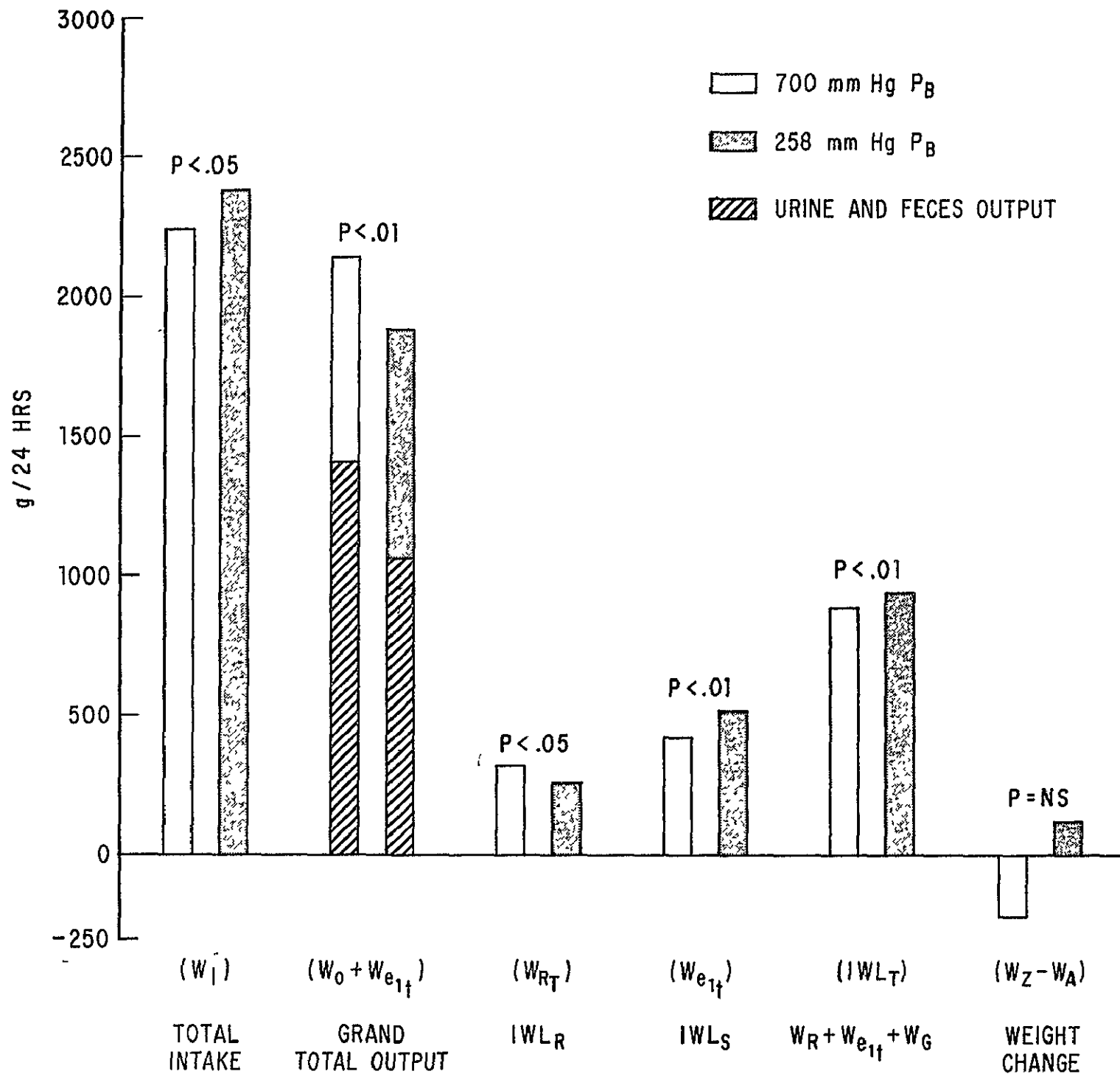


Fig. 18 Effect of water vapor pressure ( $P_{H_2O}$ ) upon weight balance and fluid loss (paired 48-hr and 24-hr experiments). Significance levels are shown.

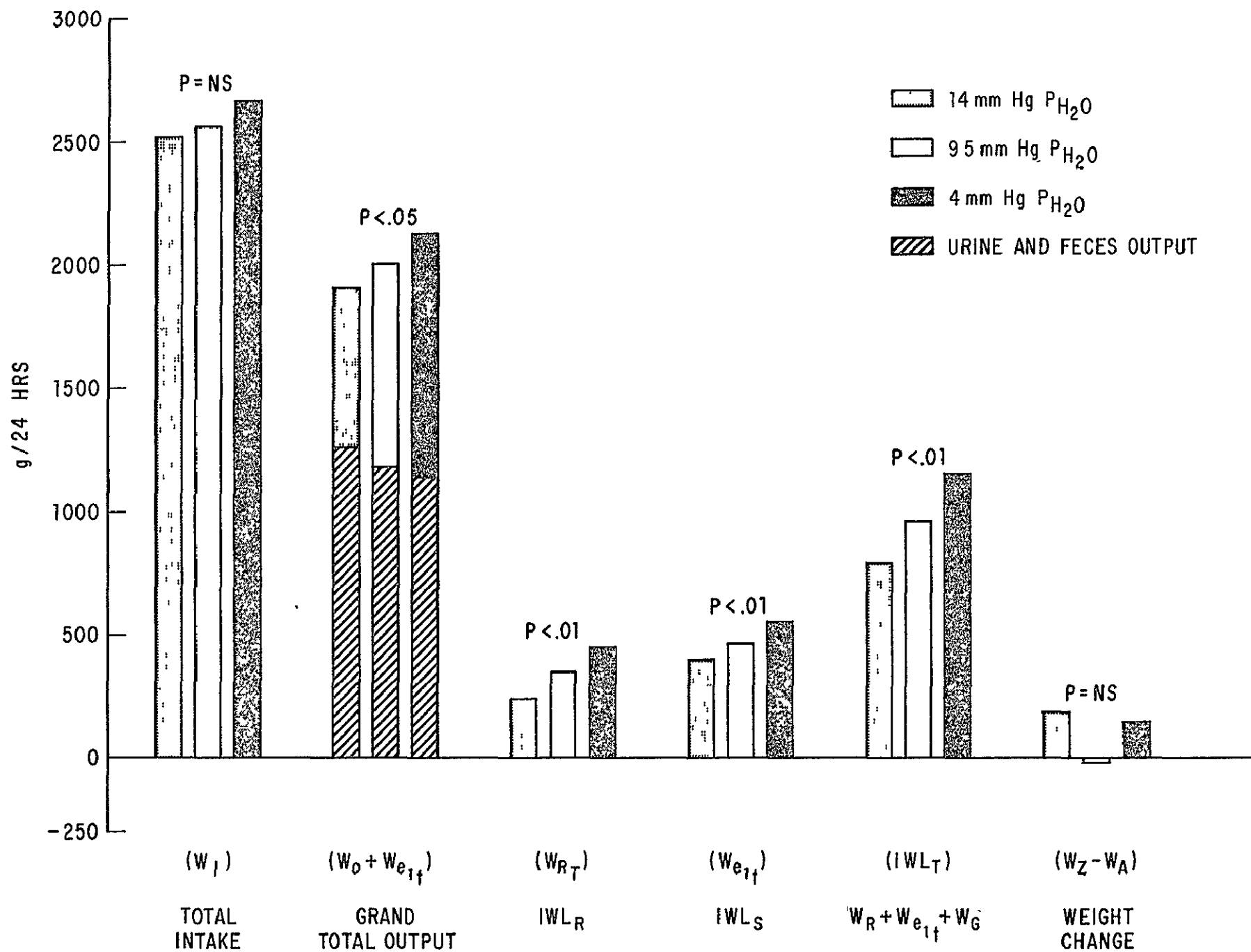


Fig. 19 Effect of ambient temperature ( $T_a$ ) upon weight balance and fluid loss (paired 48-hr and 24-hr experiments). Significance levels are shown.



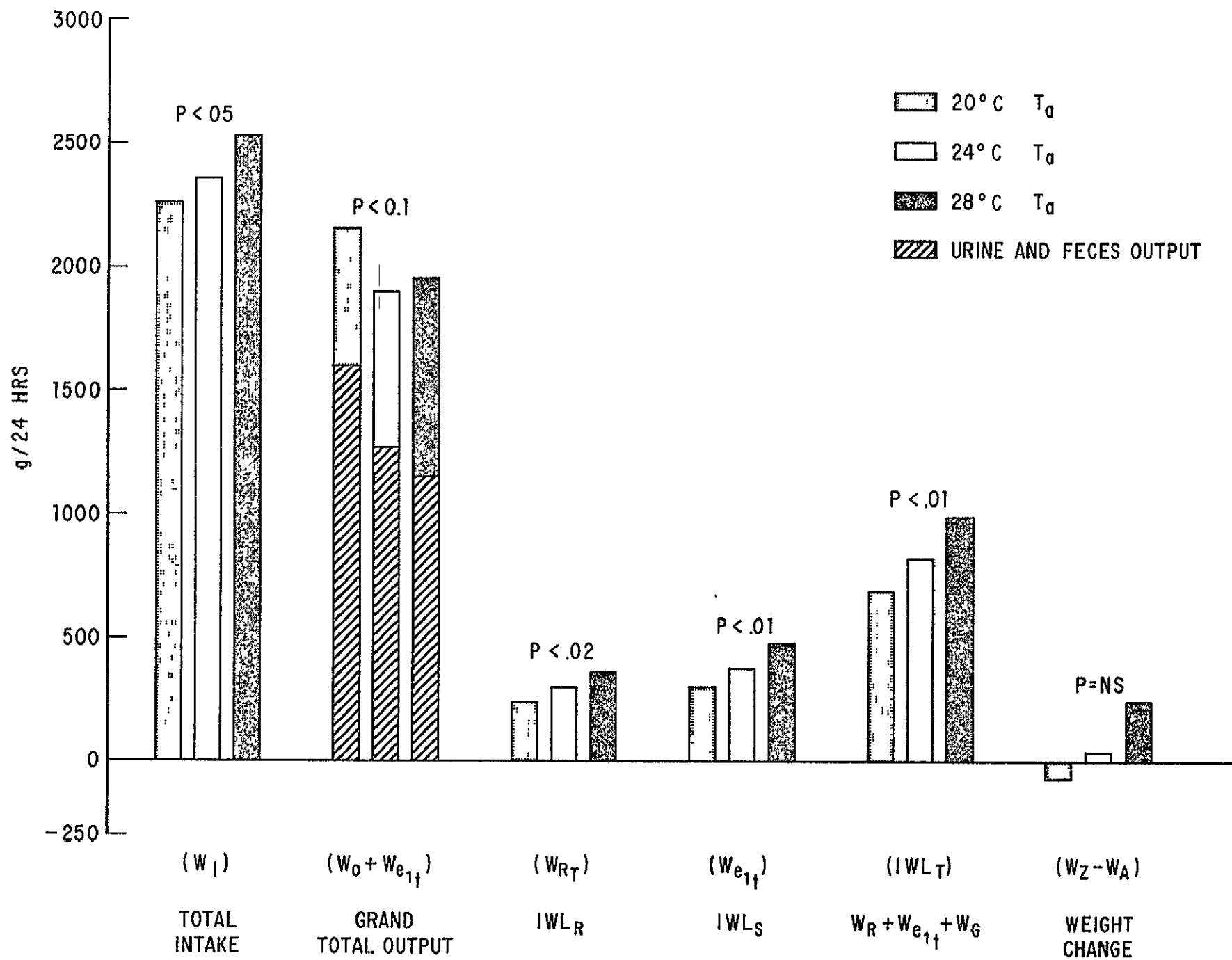


Fig. 20    Effect of gas composition (G.C.) on weight balance and fluid loss at 258 mm. Hg  $P_B$  (paired experiments). Significance levels are shown.

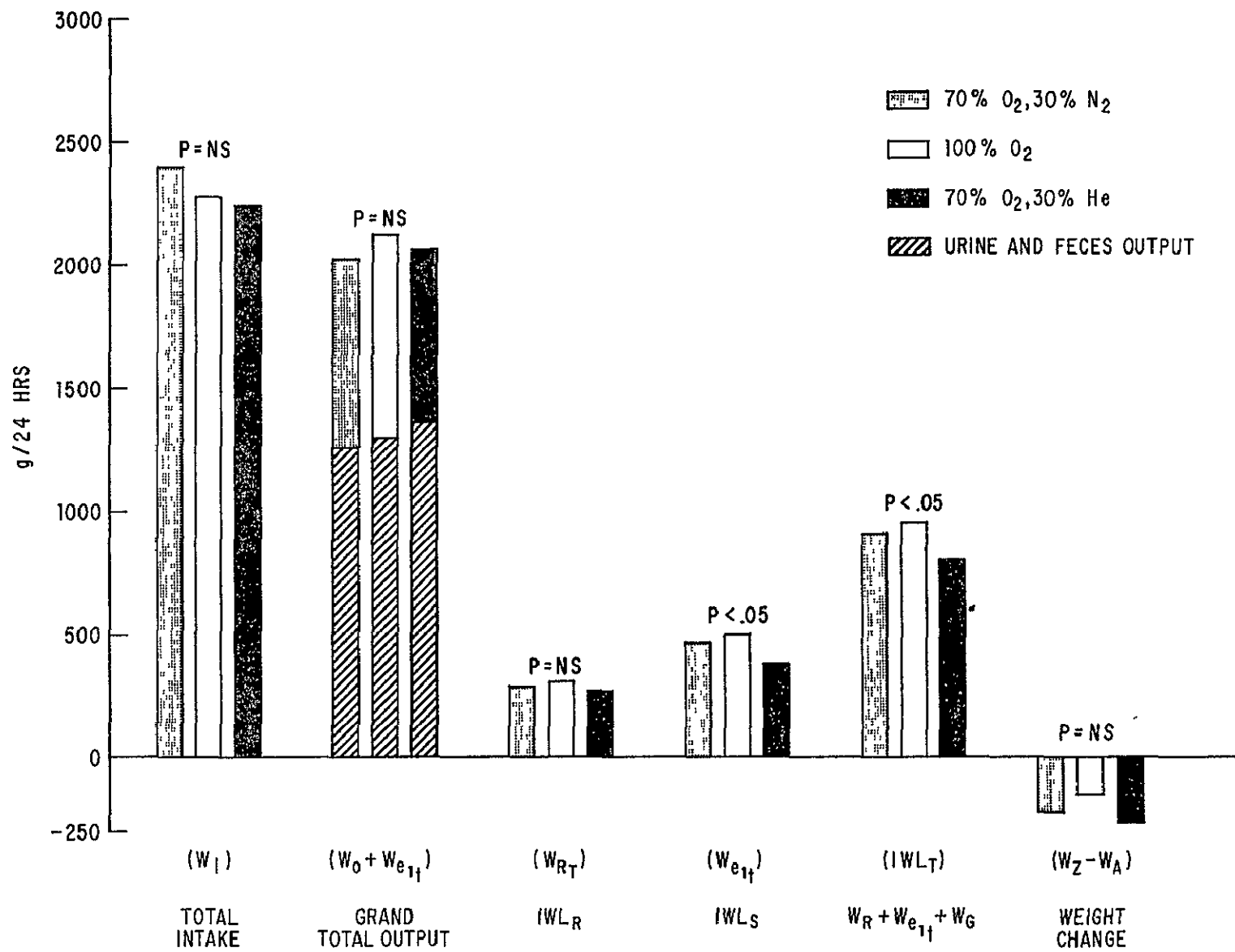


Fig. 21 Direct and indirect measurement of skin insensible weight loss ( $W_{e1t}$  and  $W_{e2t}$ ); relationship to  $P_{H_2O}$ ,  $P_B$ , and  $y$ .

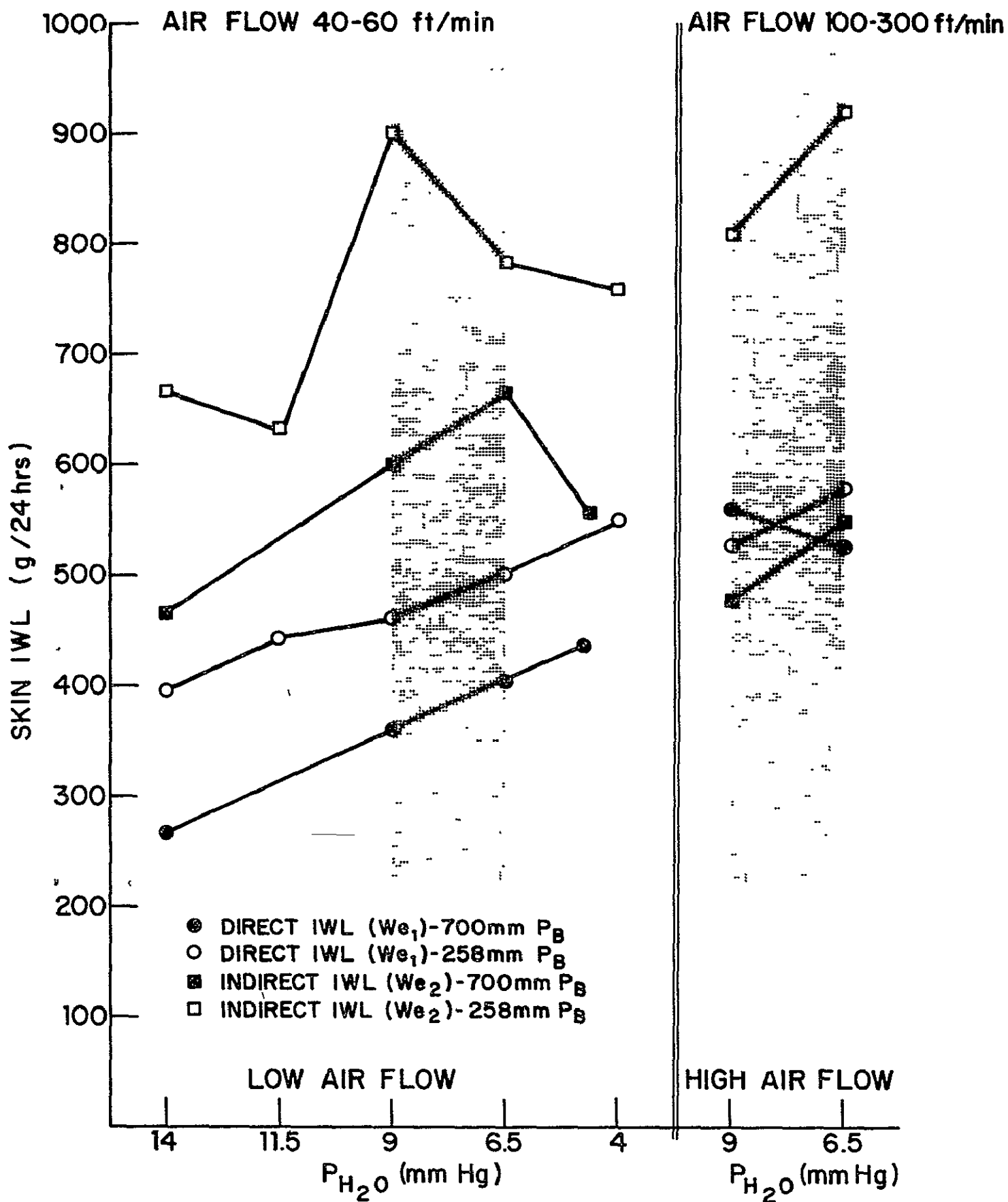


Fig. 22 Direct and indirect measurement of skin insensible weight loss ( $W_{e1t}$  and  $W_{e2t}$ ); relationship to  $T_a$  and  $P_B$ .

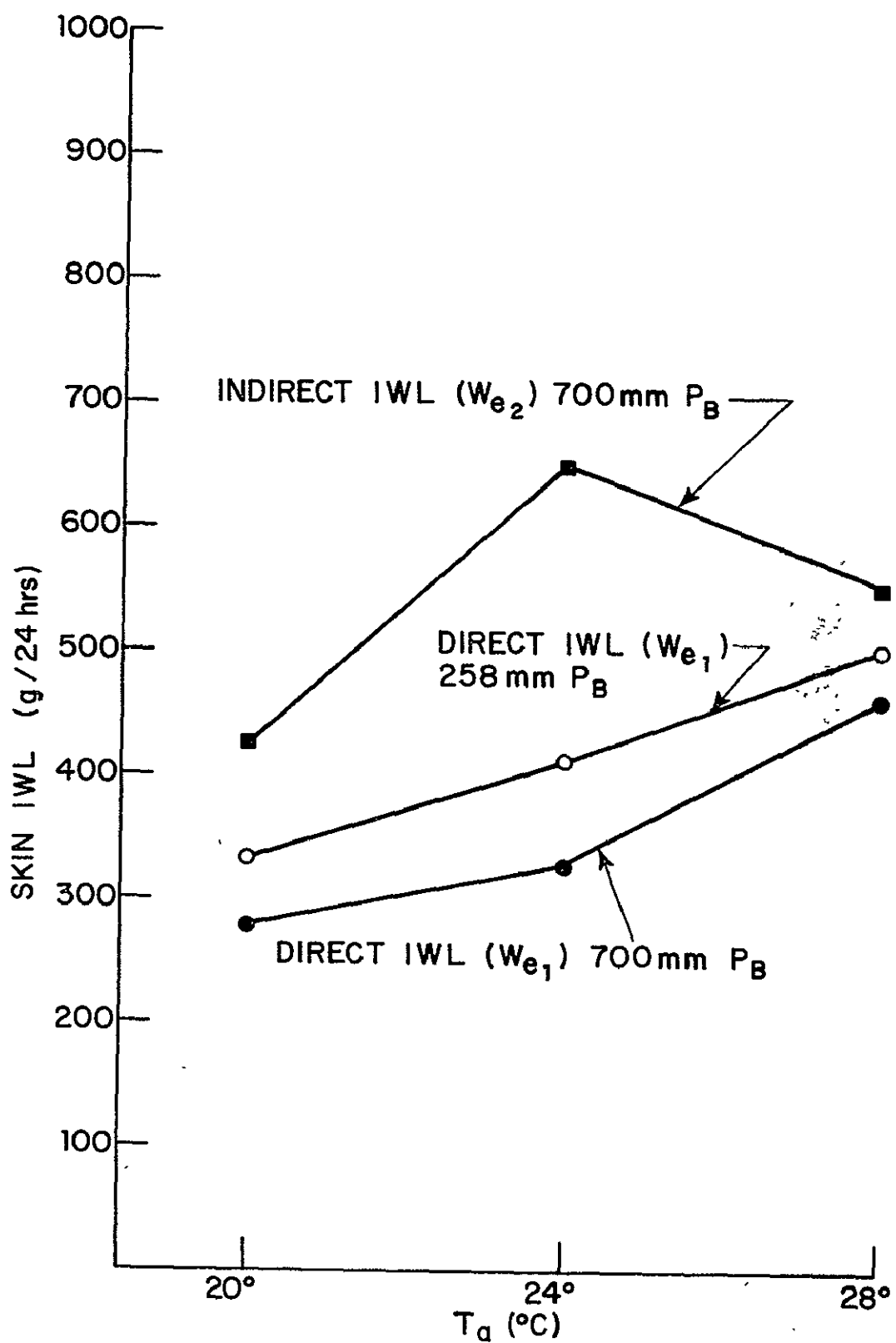


Fig. 23 Relationship of respiratory-insensible water loss ( $W_R$ ) to  $P_{H_2O}$ , R.H., and  $P_B$  at  $24^{\circ}$  C.  $T_a$ . Mean values and S.D. are shown.



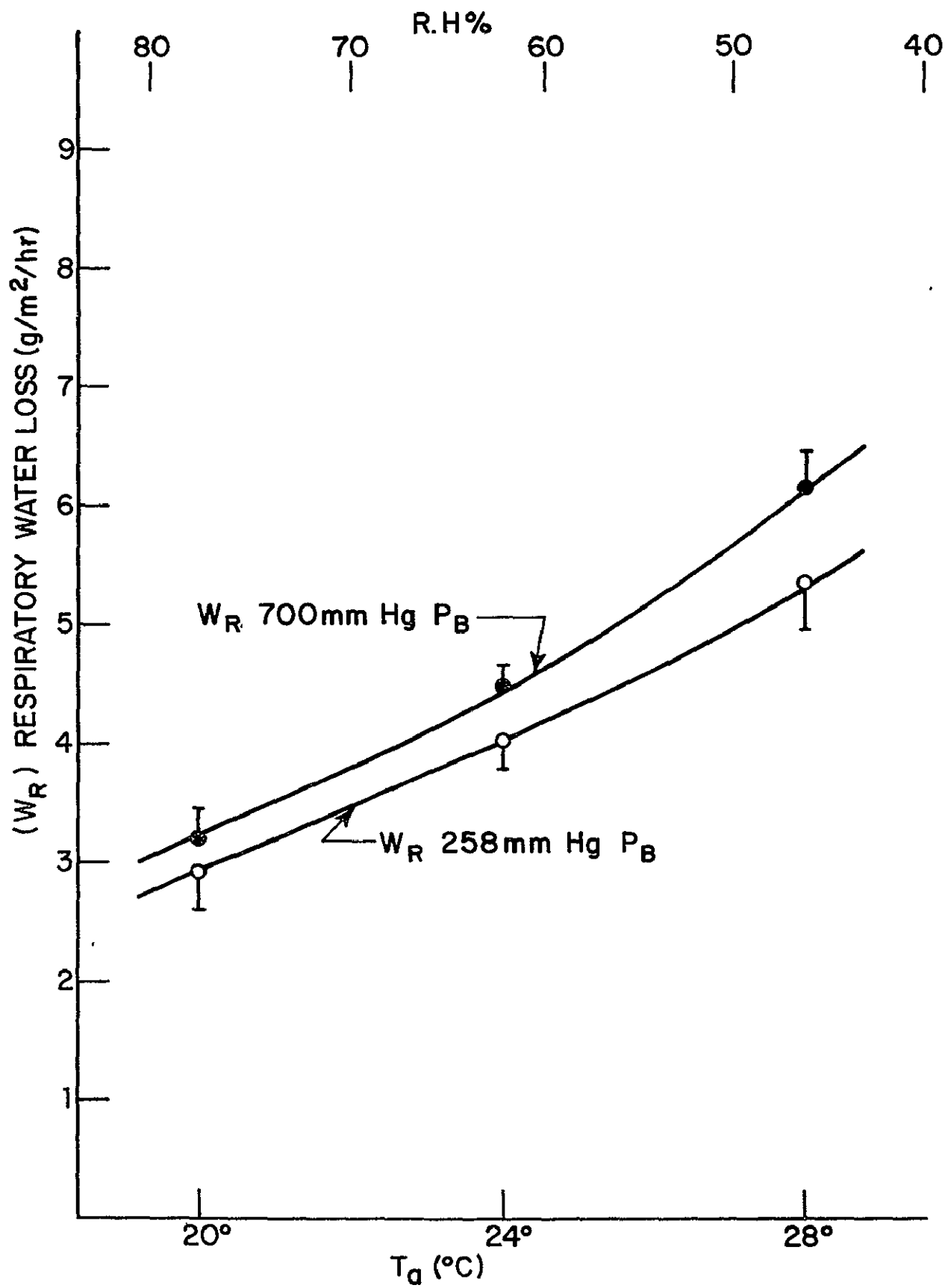


Fig. 24 Relationship of respiratory insensible water loss ( $W_R$ ) to  $T_a$ ,  $P_B$ , and R.H. at 14 mm. Hg  $P_{H_2O}$ . Mean values and S.D. are shown.

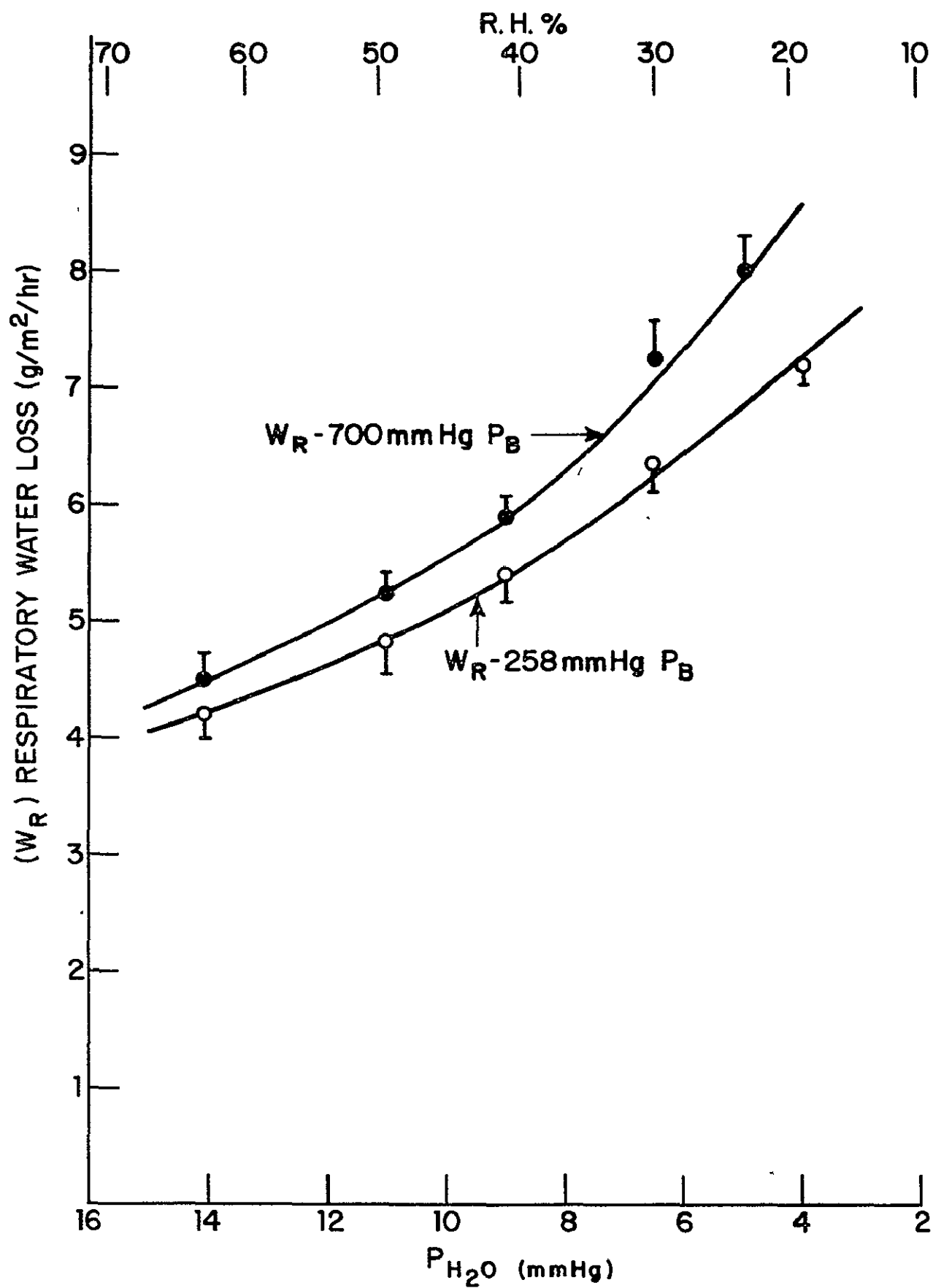


Fig. 25 Relationship of relative humidity of inspired air to rates of respiratory insensible water loss ( $\dot{W}_R$ ) at two levels of  $P_B$ . The data represent multiple values of  $T_a$  and  $P_{H_2O}$ . Average pulmonary ventilation rates for the two levels of  $P_B$  are shown.

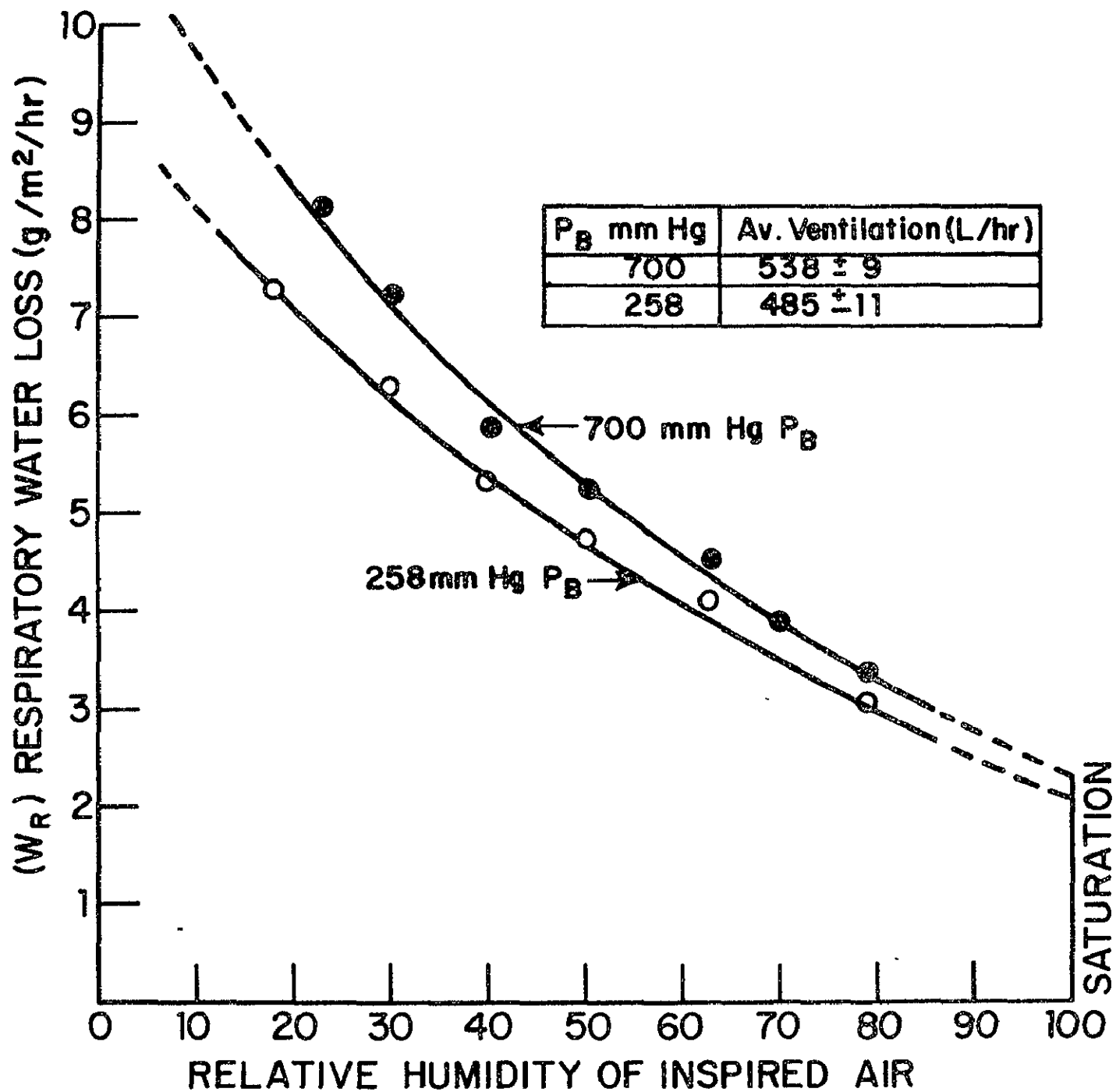


Fig. 26 Relationship of relative humidity of ambient air to rates of skin insensible weight loss ( $W_{e1}$ ) at two levels of  $P_B$ . Note the significant influence of  $\bar{T}_a$  irrespective of its role in the determination of R.H.

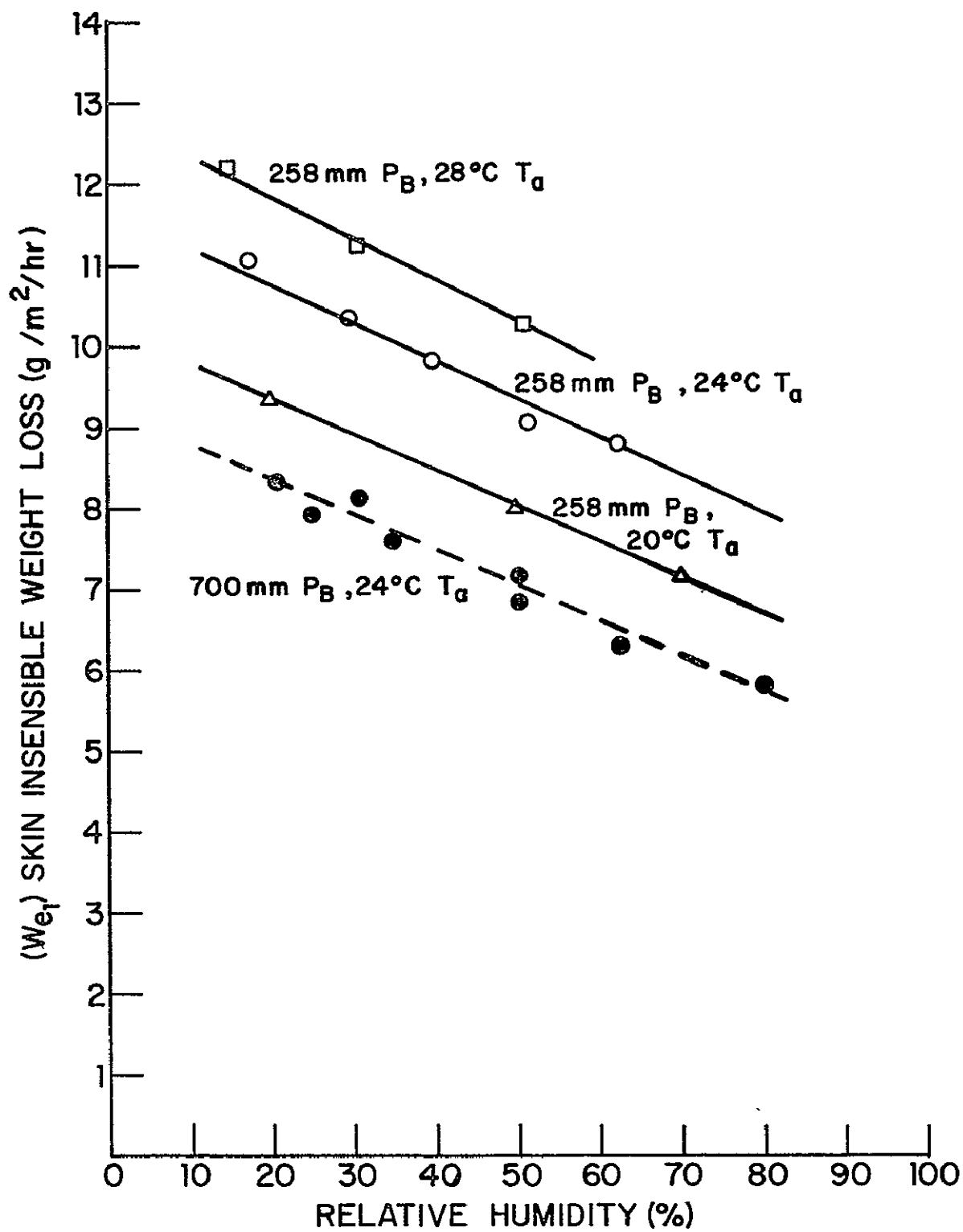


Fig. 27 Total insensible weight loss ( $IWL_T$ ) and its components, relationship to  $P_B$  and  $P_{H_2O}$  at  $24^{\circ}$  C.  $T_a$ .



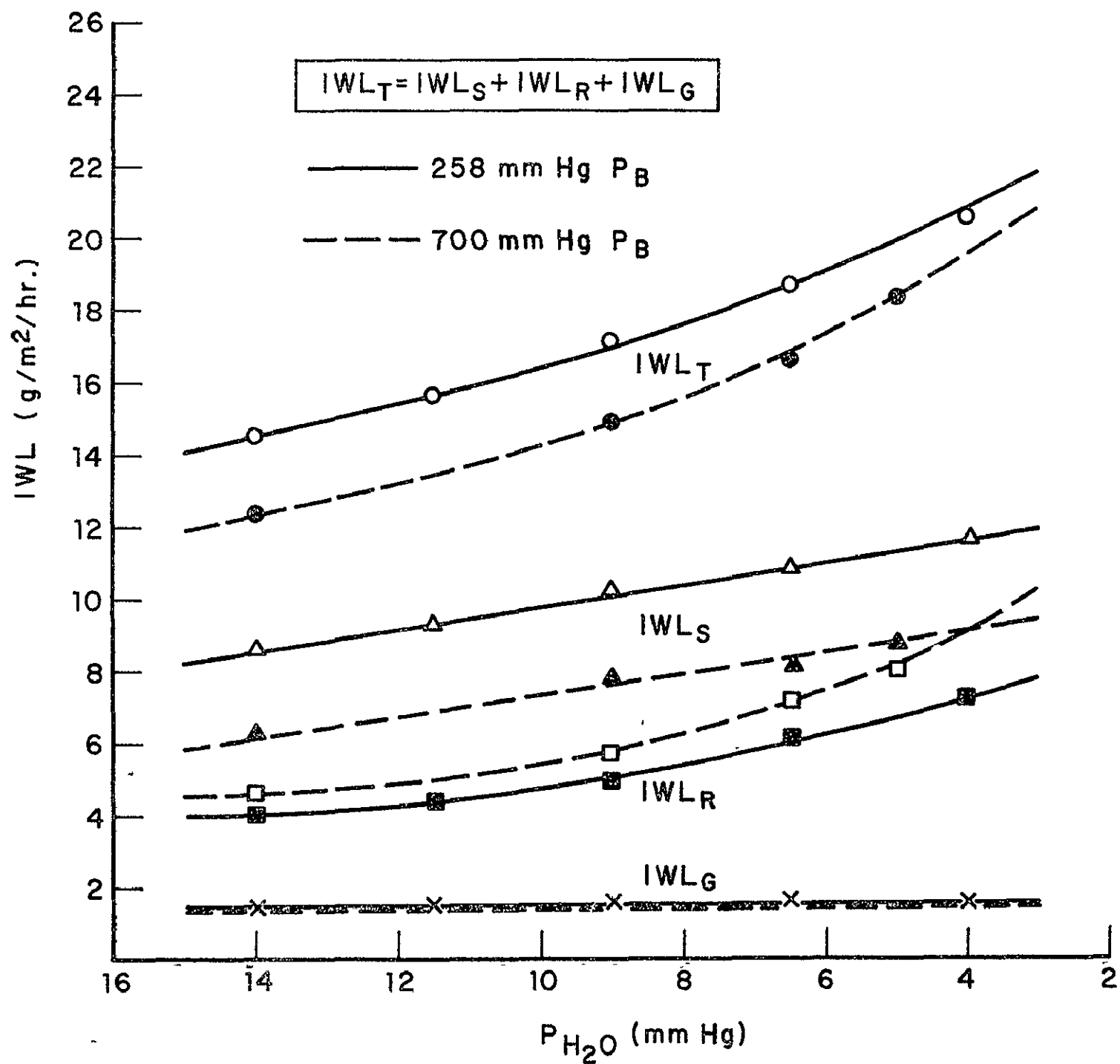


Fig. 28 Total insensible weight loss ( $IWL_T$ ) and its components;  
Relationship to  $T_a$  and  $P_B$  at 14 mm Hg  $P_B$ .

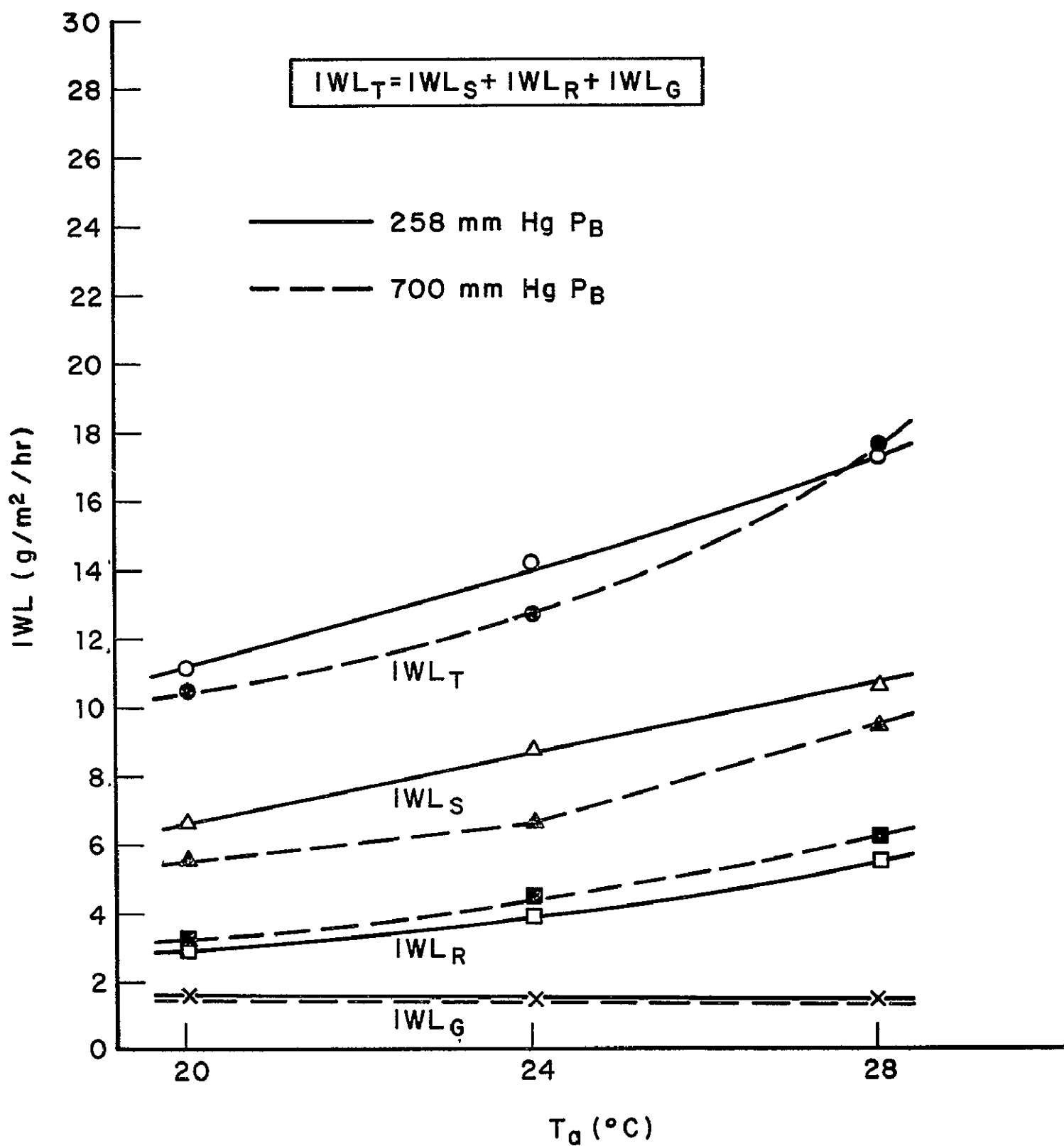
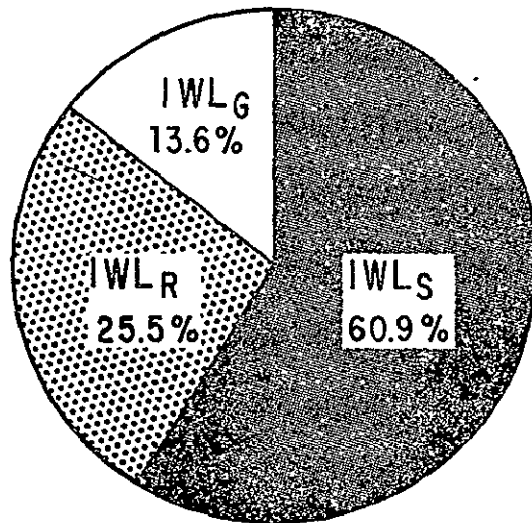


Fig. 29    Components of  $IWL_T$ ; the varying contributions of  $IWL_S$ ,  $IWL_R$ , and  $IWL_G$ . Note that  $IWL_S$  is always the most important.

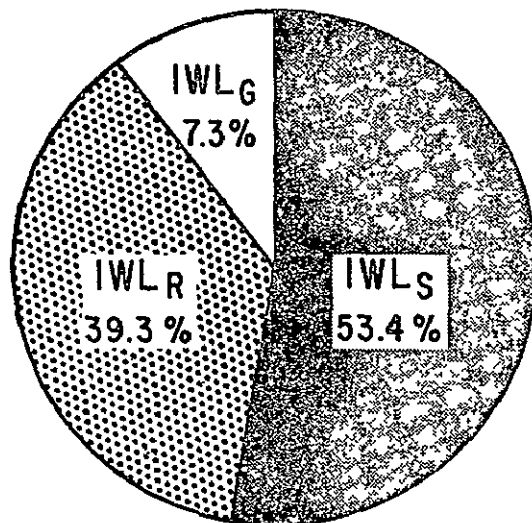
# AMBIENT CONDITIONS



258 mm Hg  $P_B$

14 mm Hg  $P_{H_2O}$

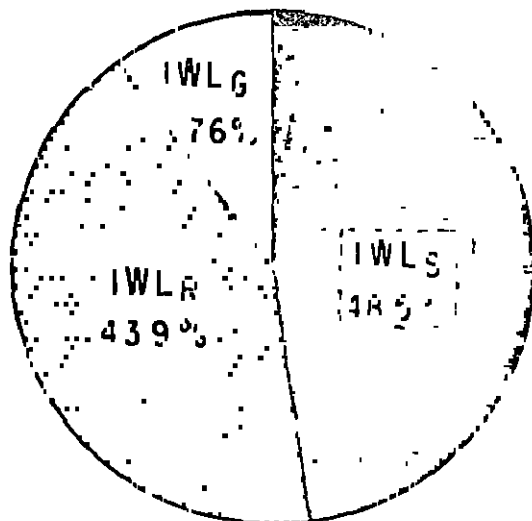
20°C  $T_a$



700 mm Hg  $P_B$

9 mm Hg  $P_{H_2O}$

24°C  $T_a$



700 mm Hg  $P_B$

5 mm Hg  $P_{H_2O}$

24°C  $T_a$

Fig. 30 Sign and symptom development; relationship to  $P_{H_2O}$  and  $P_B$   
(all experiments 24-hr duration).

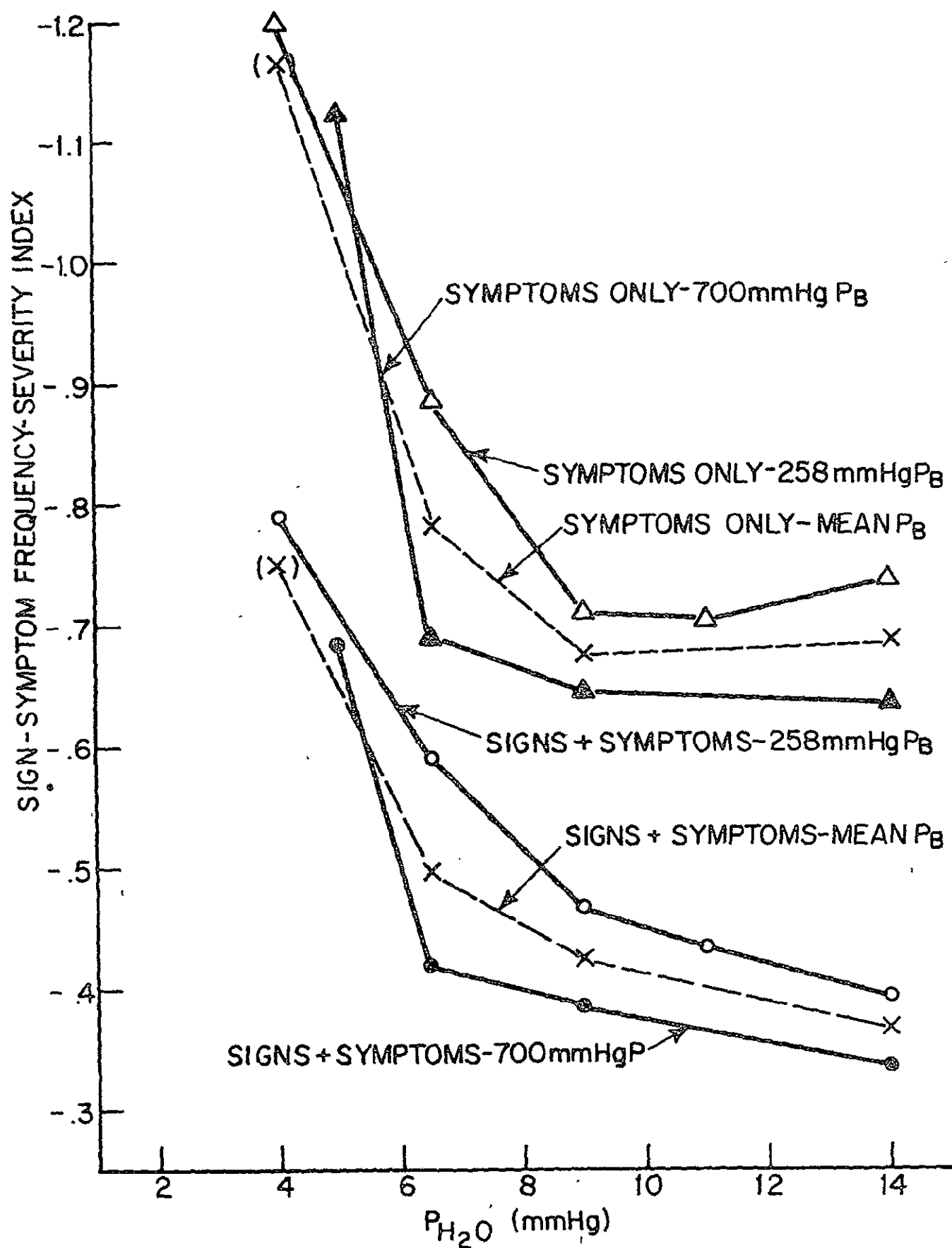


Fig. 31 Sign and symptom development; relationship to  $\dot{P}_{H_2O}$  and  $P_B$   
(48-hr experiments only).



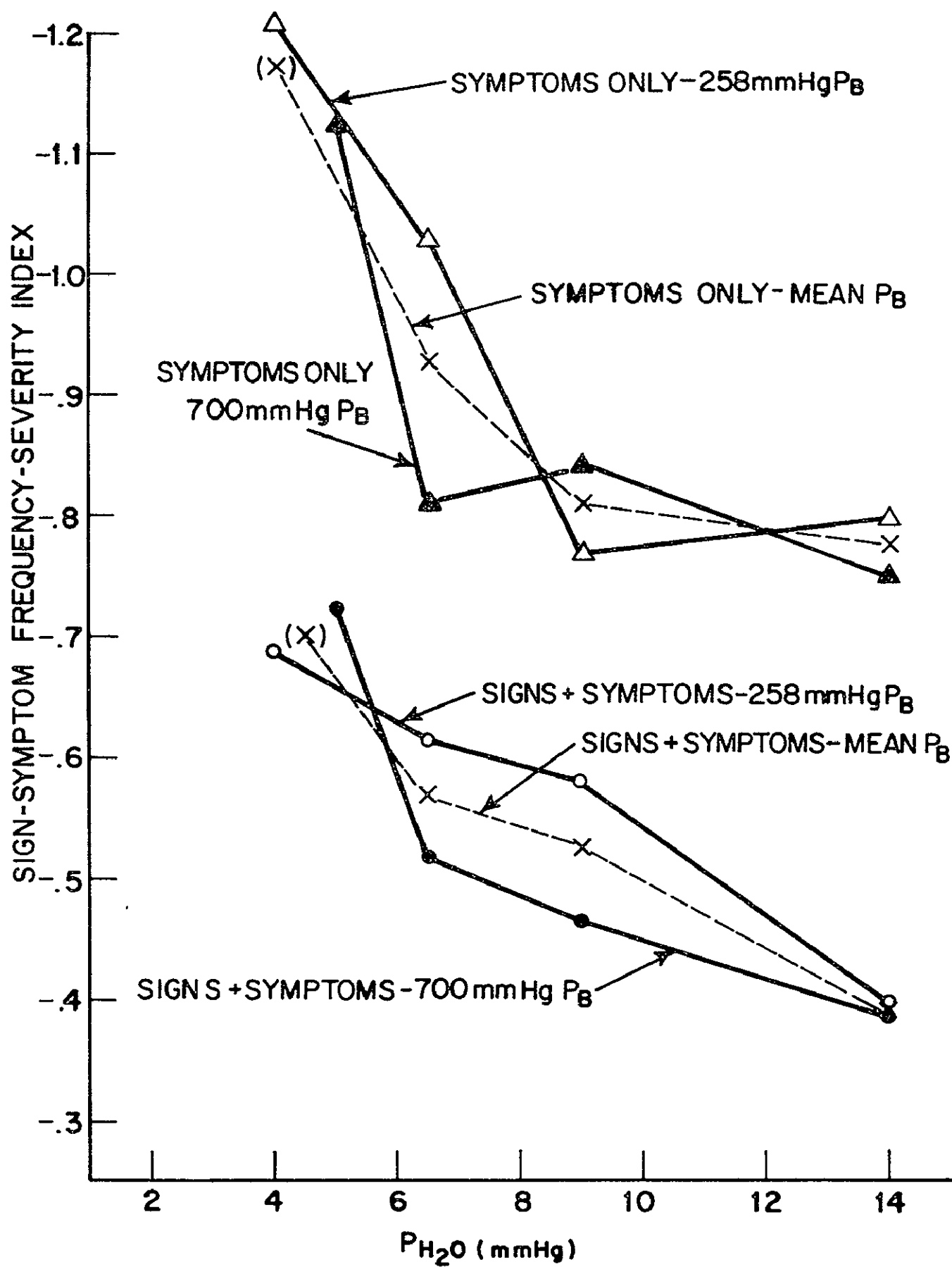


Fig. 32    Sign and symptom development; relationship to  $T_a$  and  $P_B$   
(48-hr. experiments only).

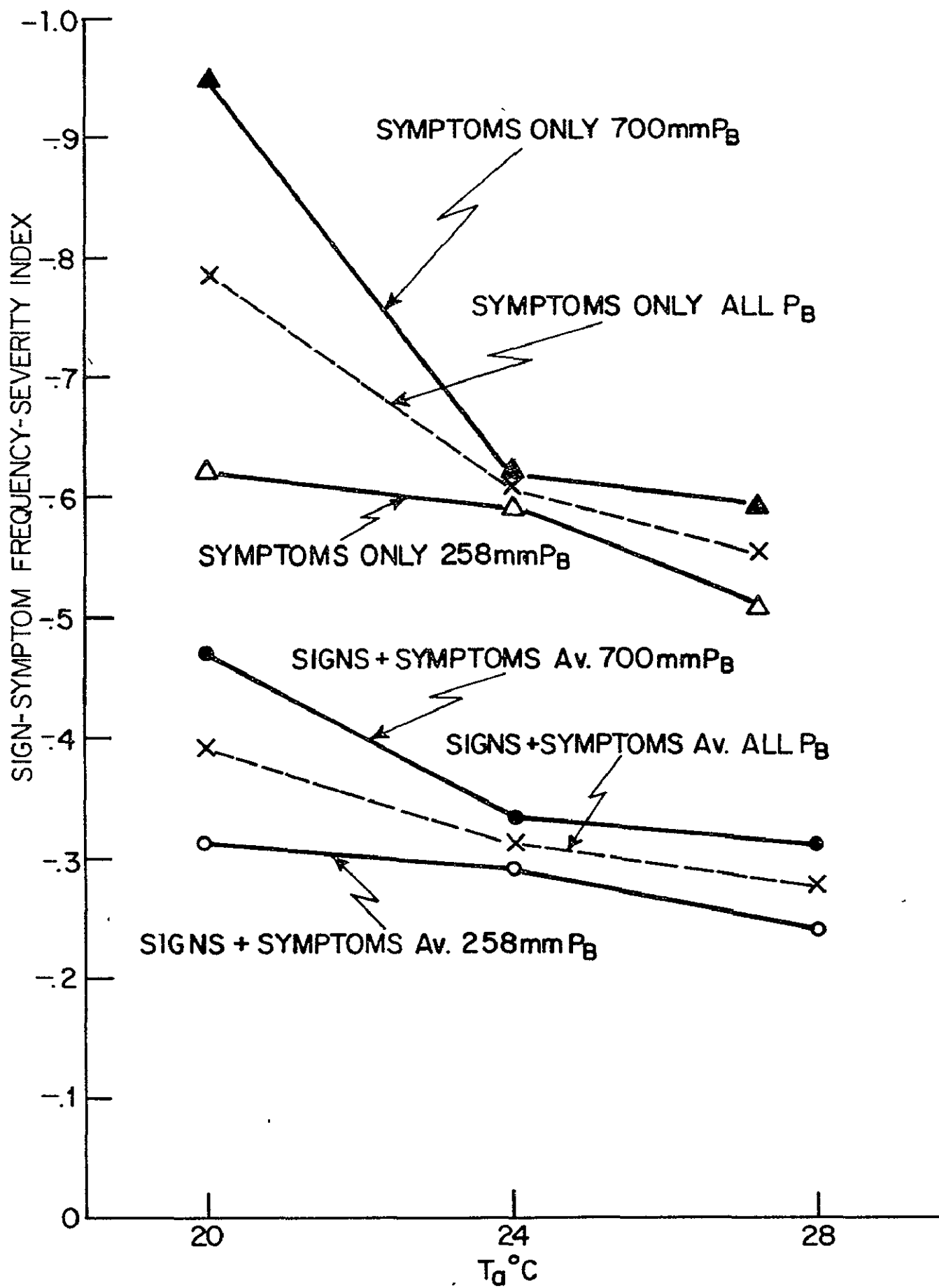


Fig. 33 Time course of symptom development at 4-5 mm and at 14 mm Hg.  $P_{H_2O}$  (48-hr experiments at  $24^{\circ}$  C.  $T_a$ ). The influence of total pressure is also demonstrated.

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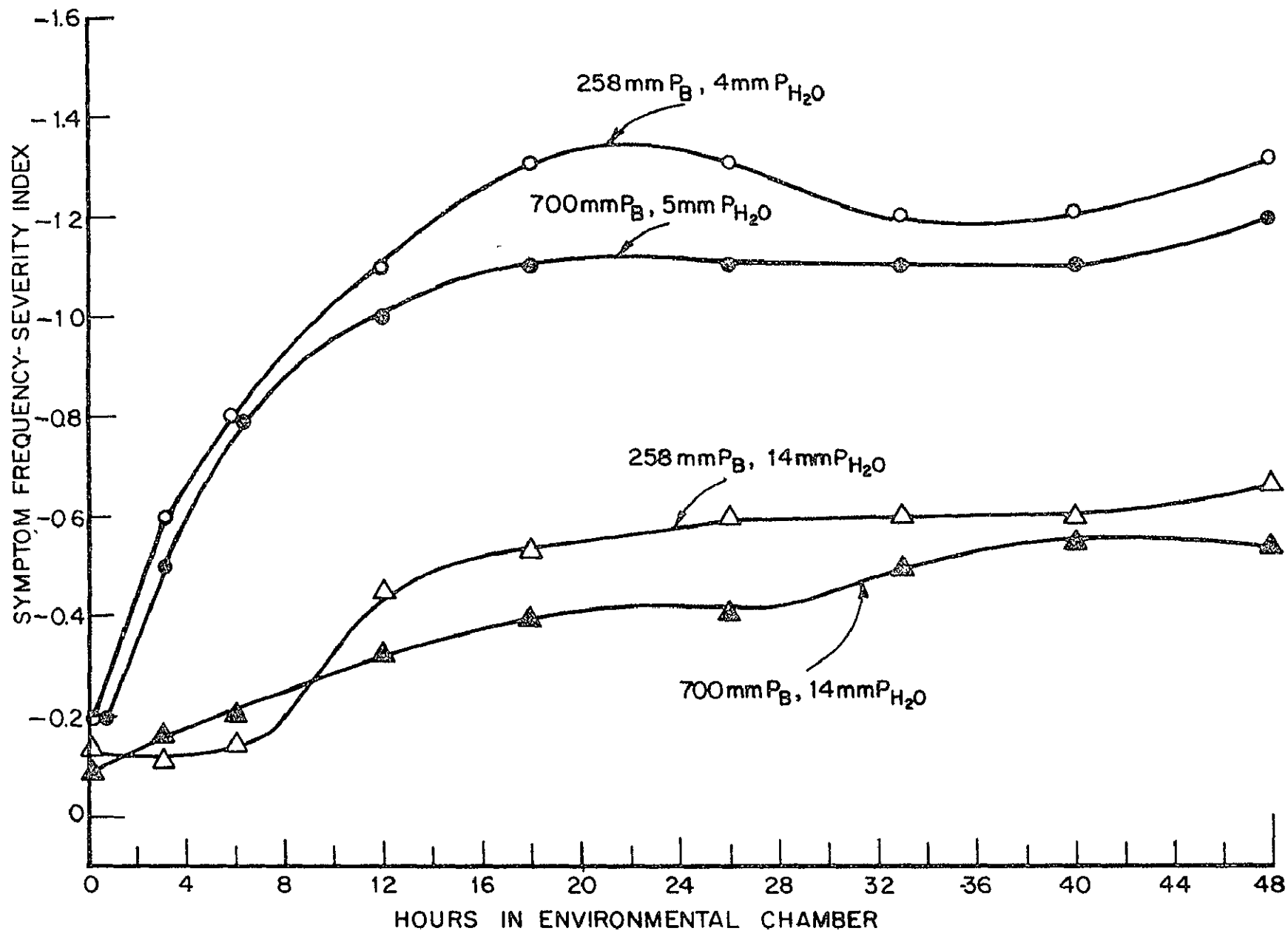


Fig. 34 Time course of symptom development at 6.5 mm and 9 mm Hg  $P_{H_2O}$  (48-hr experiments at 24° C.  $T_a$ ). The influence of  $P_E$  is again demonstrated.

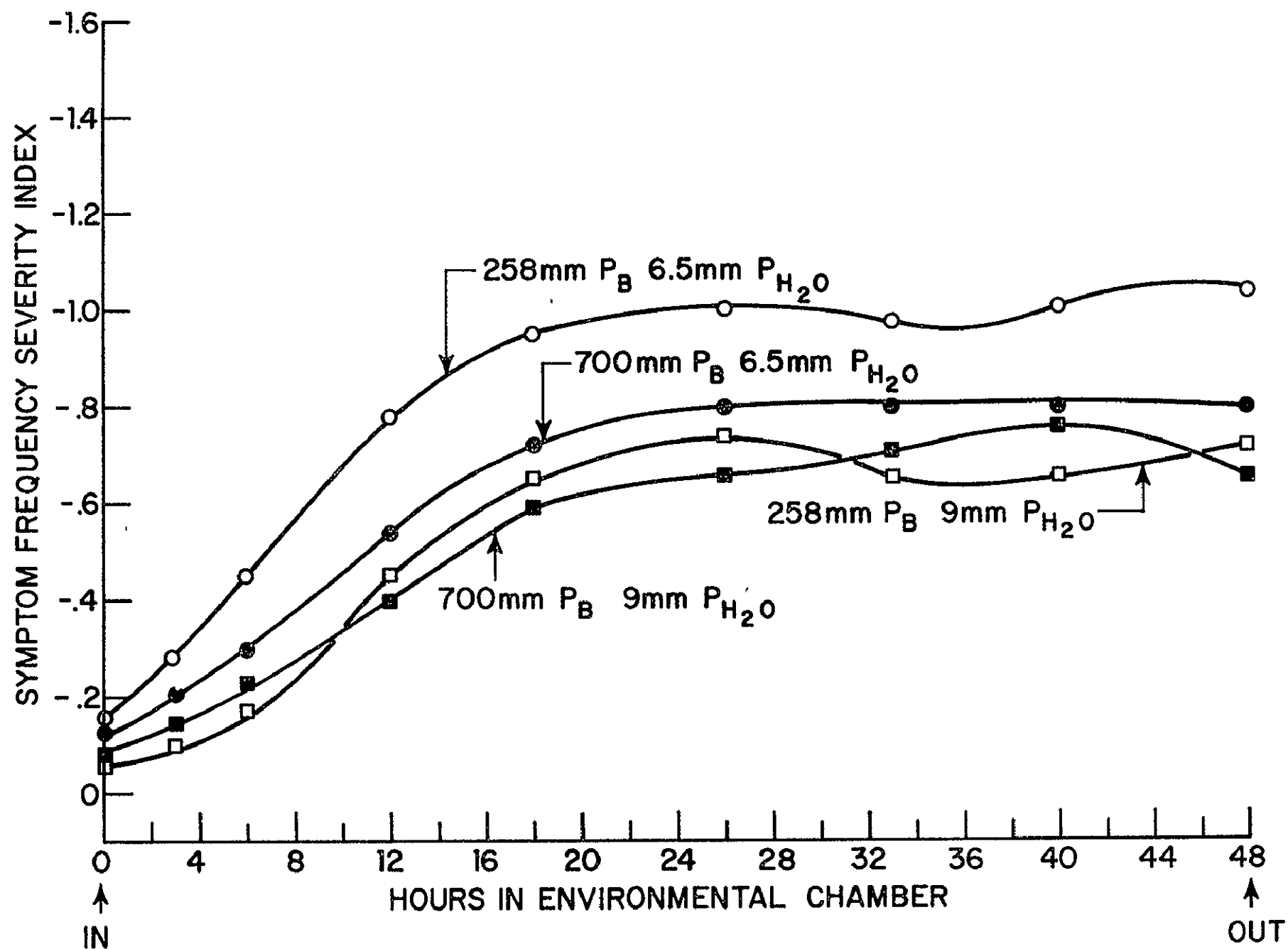


Fig. 35 Time course of sign development at 4-5 mm and 14 mm Hg.  
 $P_{H_2O}$  (48-hr experiments at 24° C.  $T_a$ ). The  $P_B$  effect is  
also seen.



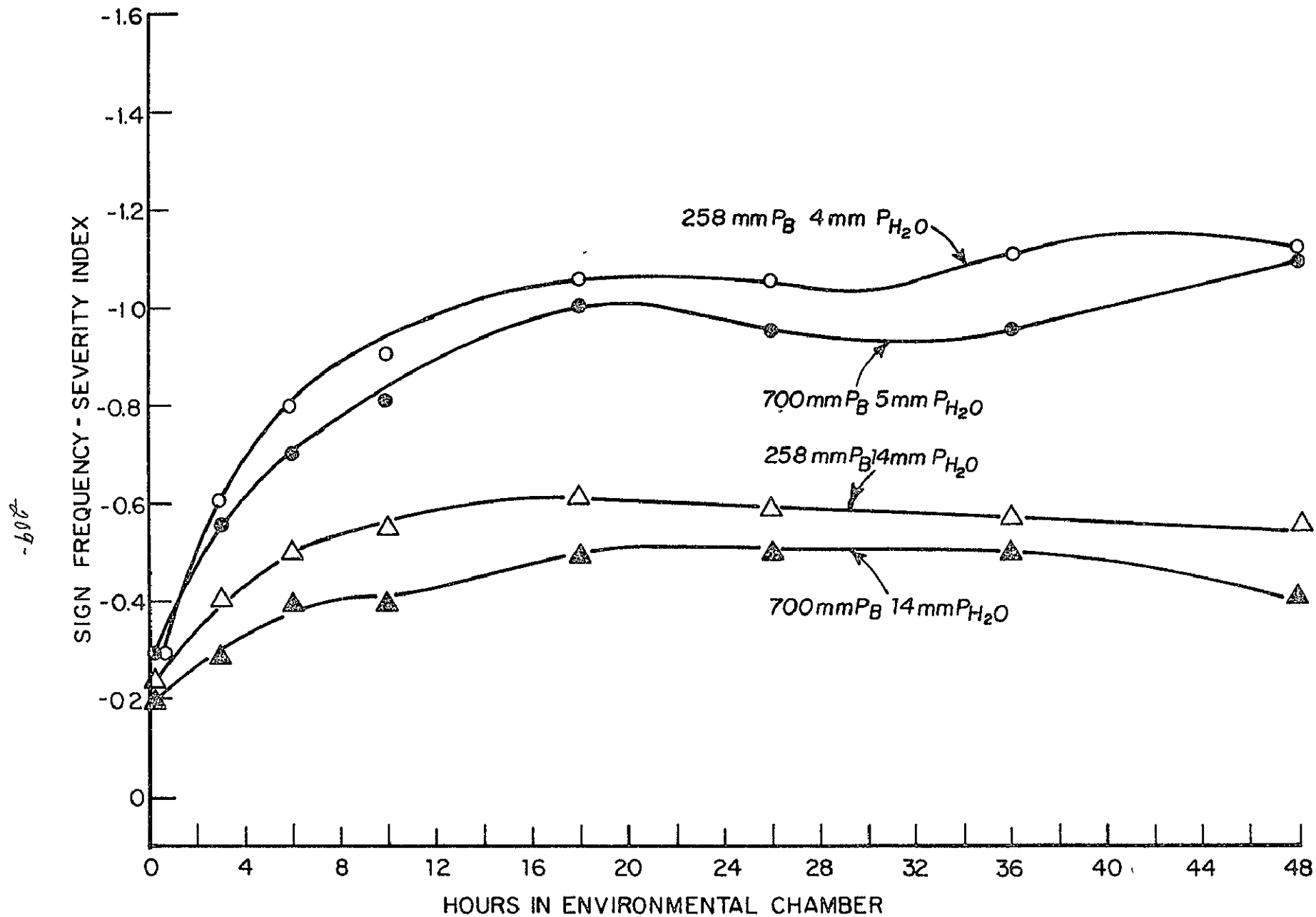


Fig. 36 Time course of sign development at 6.5 mm and 9 mm Hg.  $P_{H_2O}$   
(48-hr. experiments at  $24^{\circ}$  C.  $T_a$ ). The  $P_B$  effect is again  
seen.

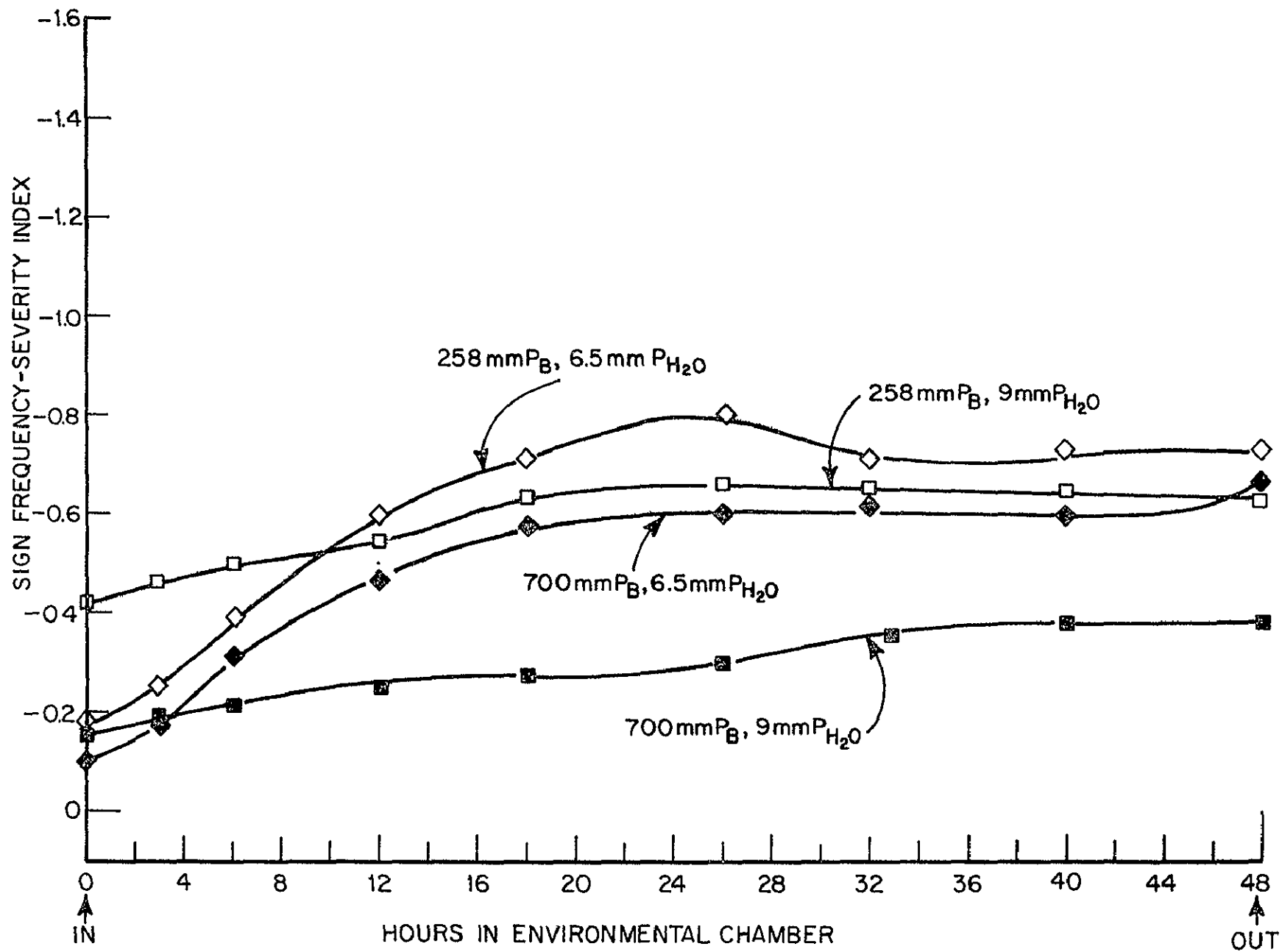


Fig. 37    Frequency-severity of symptoms related to the environment  
by anatomical areas involved, summary of all experiments.

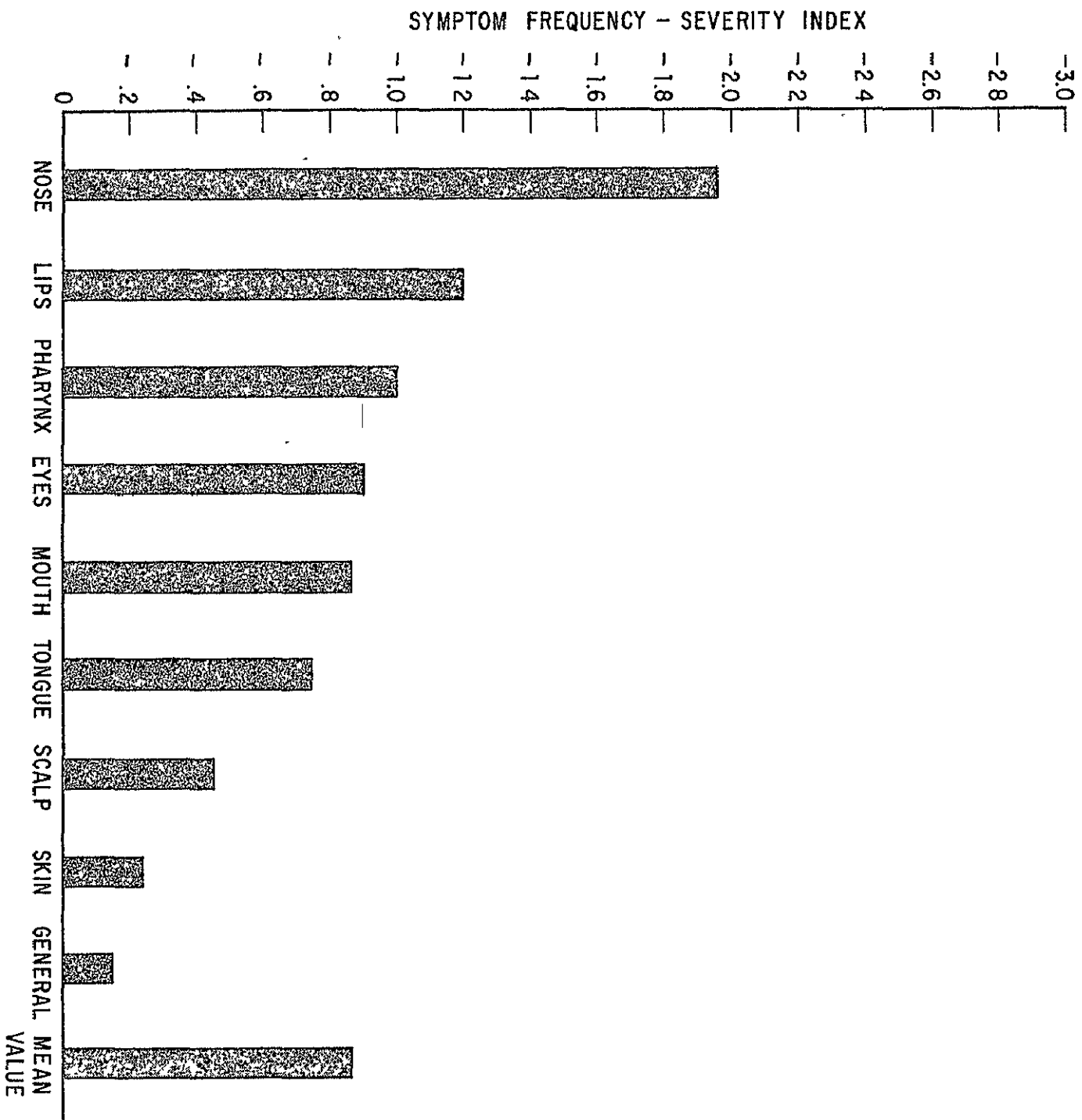


Fig. 38    Frequency-severity of symptoms related to the environment.  
Effect of  $P_B$  at  $24^{\circ}$  C.  $T_a$  (paired 24-hr and 48-hr experiments)

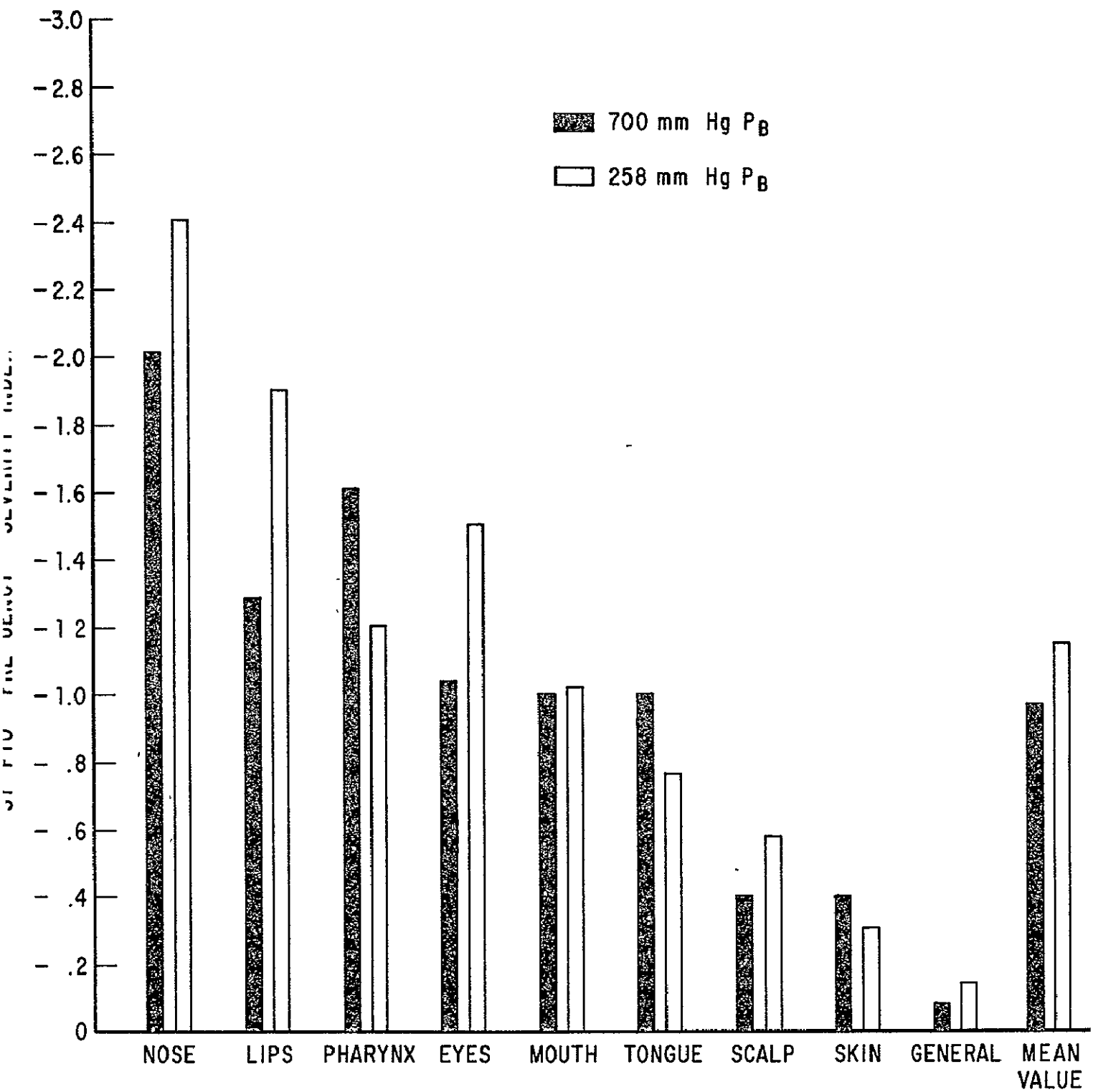


Fig. 39    Frequency-severity of symptoms related to the environment.  
Effect of  $P_{H_2O}$  at  $24^{\circ}$  C.  $T_a$  (matched 24-hr and 48-hr  
experiments).



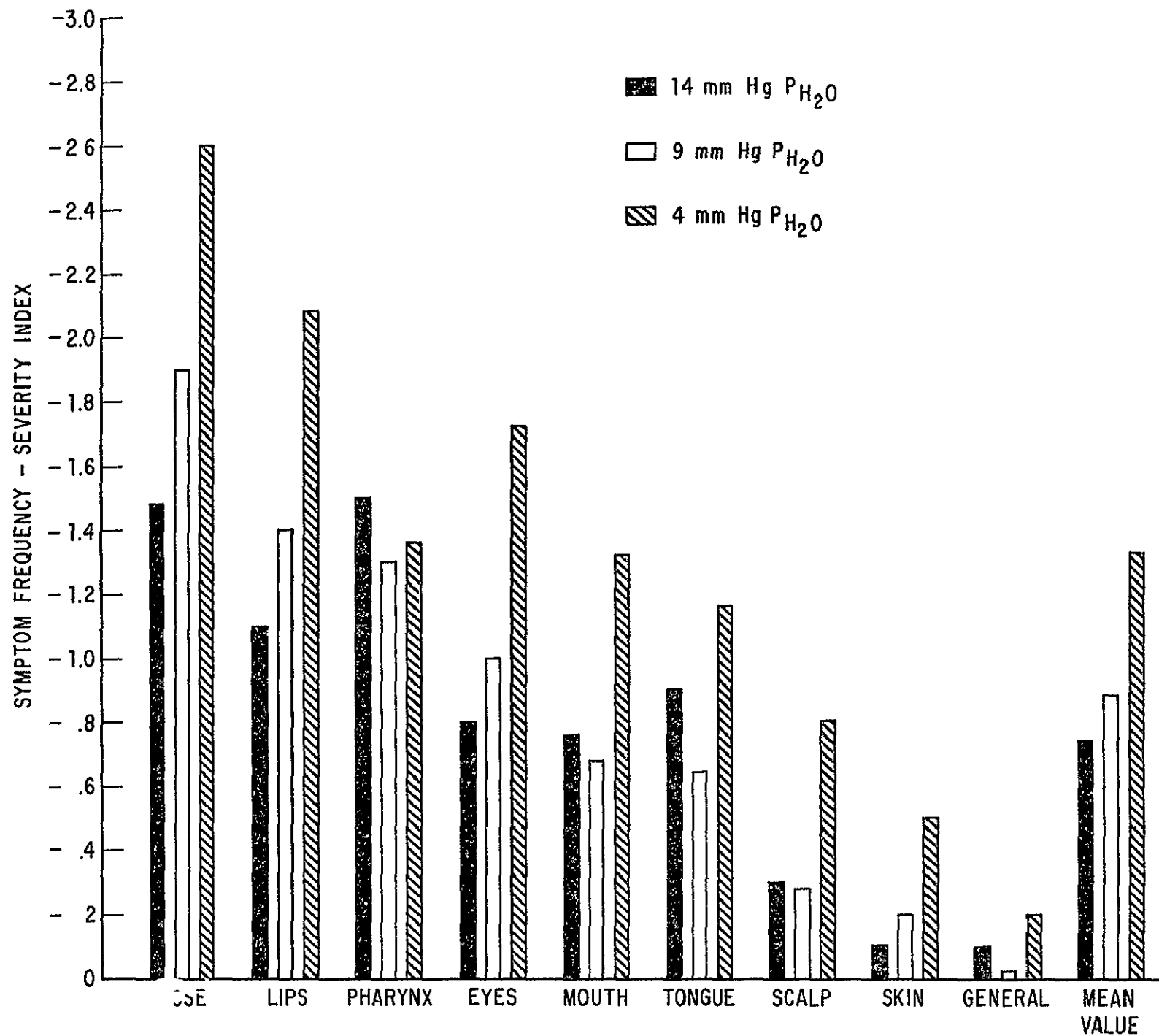


Fig. 40 Frequency-severity of symptoms related to the environment.  
Effect of  $T_a$  at 700 mm Hg  $P_B$  (matched 24-hr and 46-hr  
experiments).

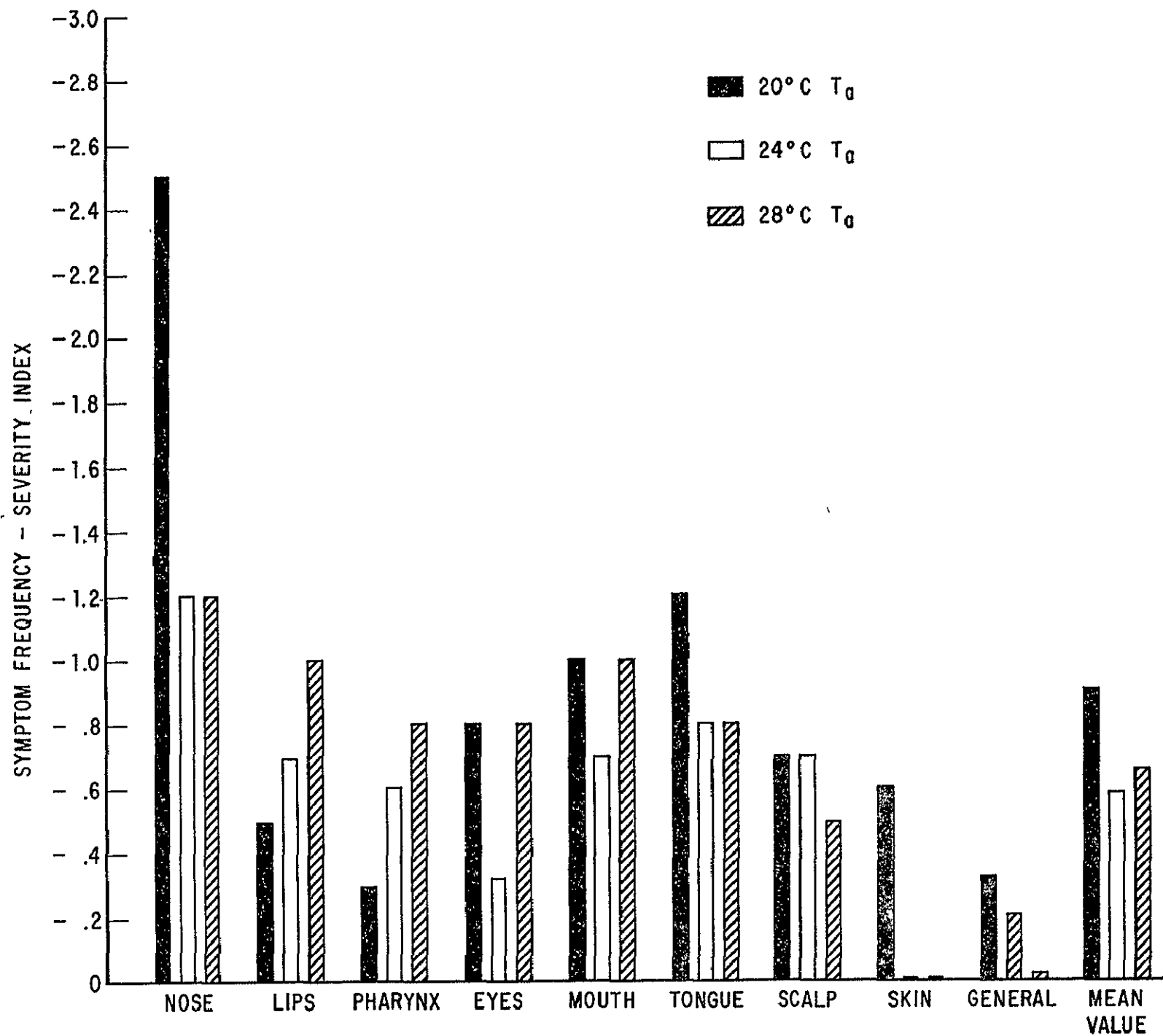


Fig. 41 Frequency-severity of symptoms related to the environment.  
Effect of gas composition at 258 mm Hg  $P_B$ , 24° C.  $T_a$   
(matched 24-hr and 48-hr experiments).

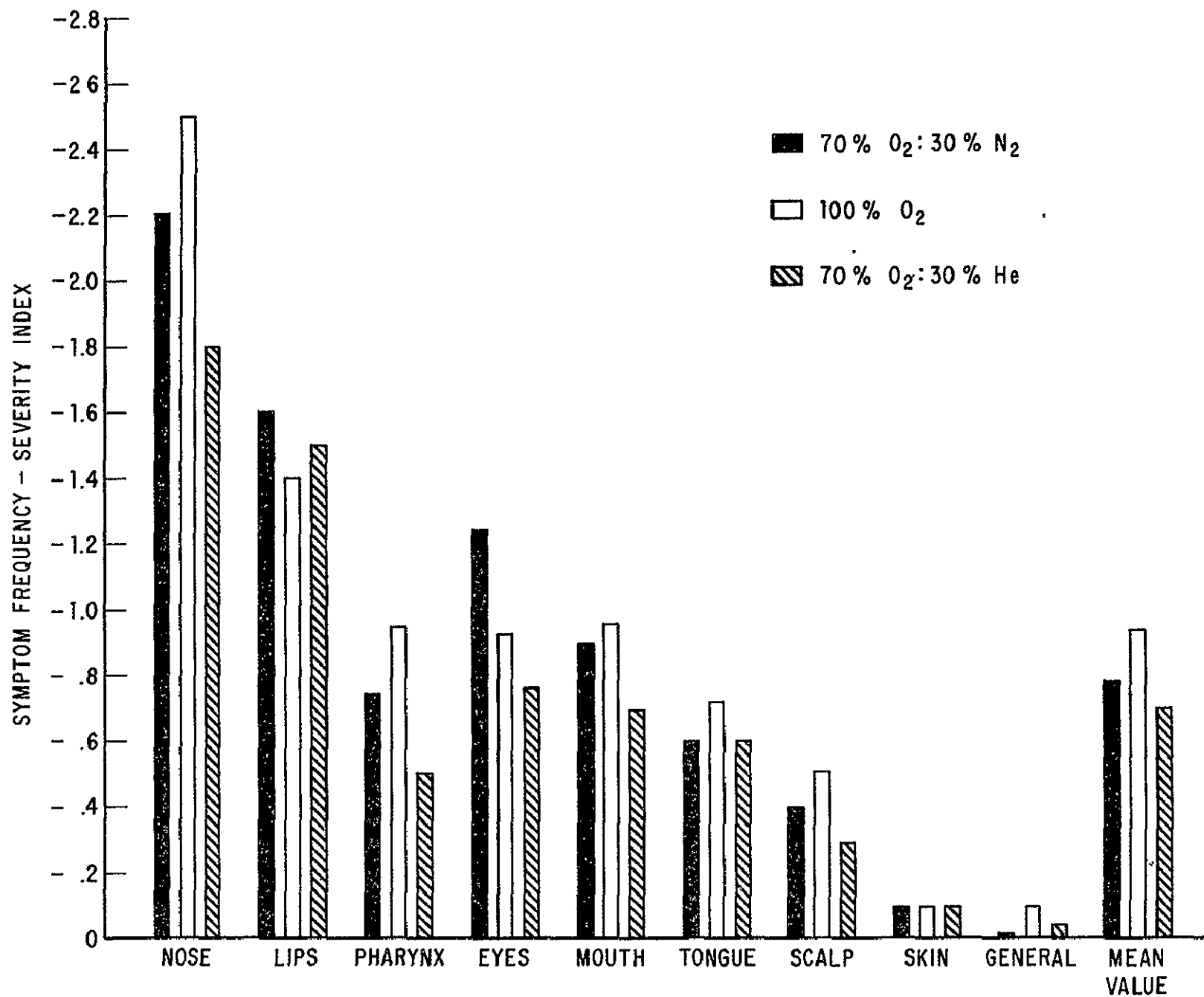


Fig. 42    Frequency-severity of signs related to the environment by anatomical area involved; summary of all experiments. Physician and subject evaluations are shown separately together with a mean value for the two.

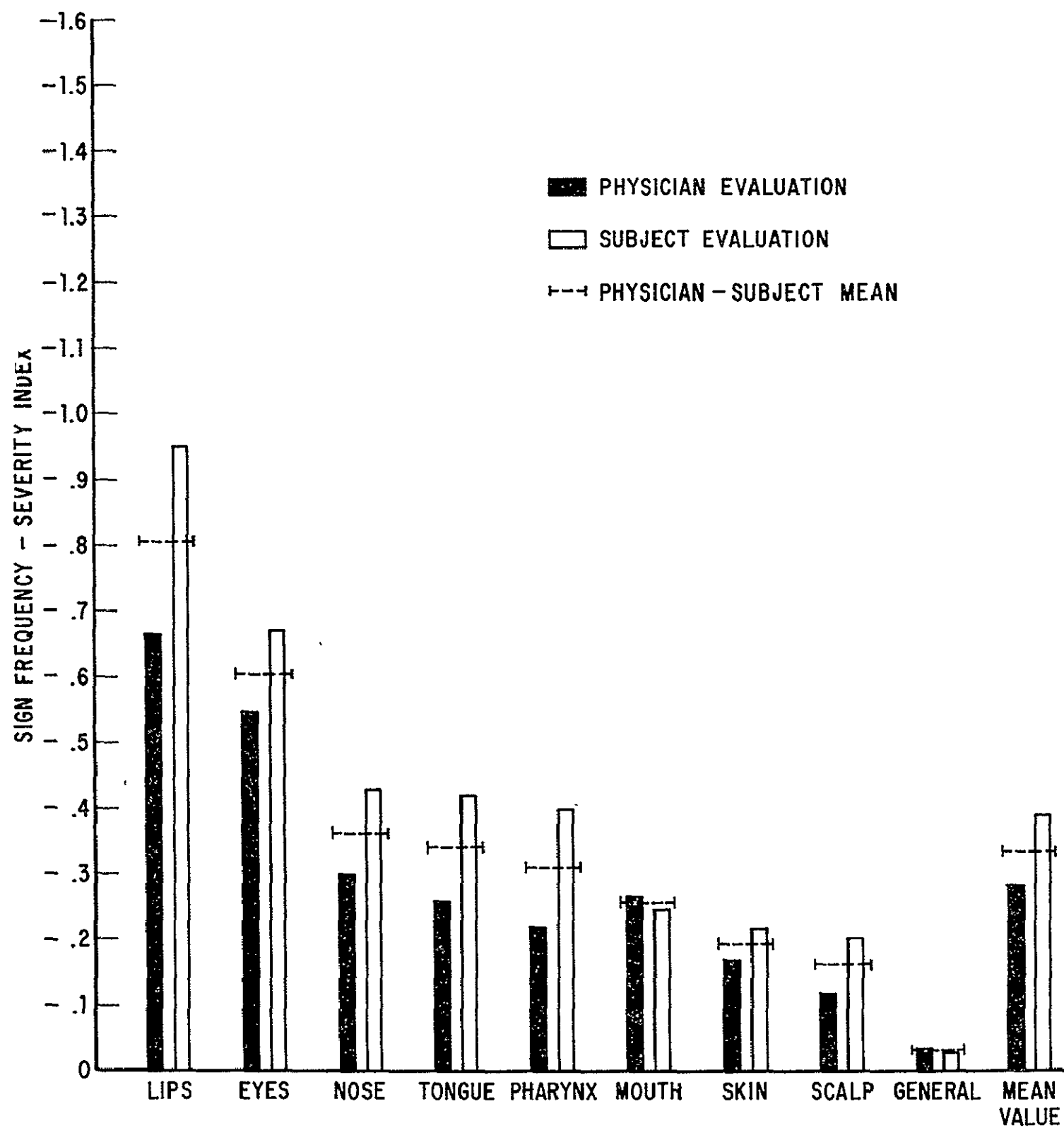


Fig. 43    Frequency-severity of signs related to the environment.  
Effect of  $P_B$  at  $24^{\circ} C. T_a$  (paired 24-hr and 48-hr experiments). Physician and subject evaluations are again shown separately.



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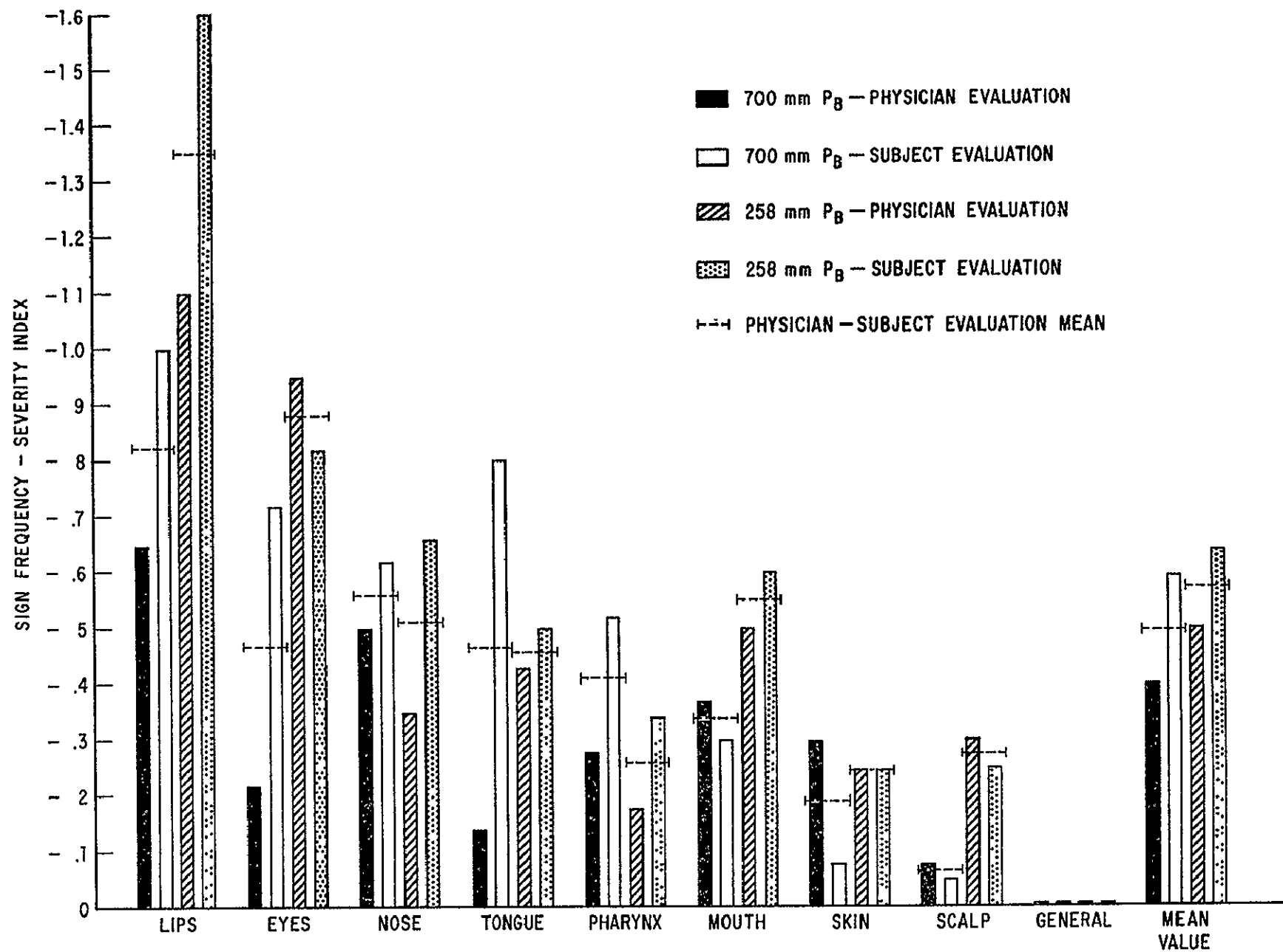


Fig. 44 Frequency-severity of signs related to the environment.  
Effect of  $P_{H_2O}$  at  $24^{\circ}$  C.  $T_a$  (matched 24-hr and 48-hr  
experiments).

-227-

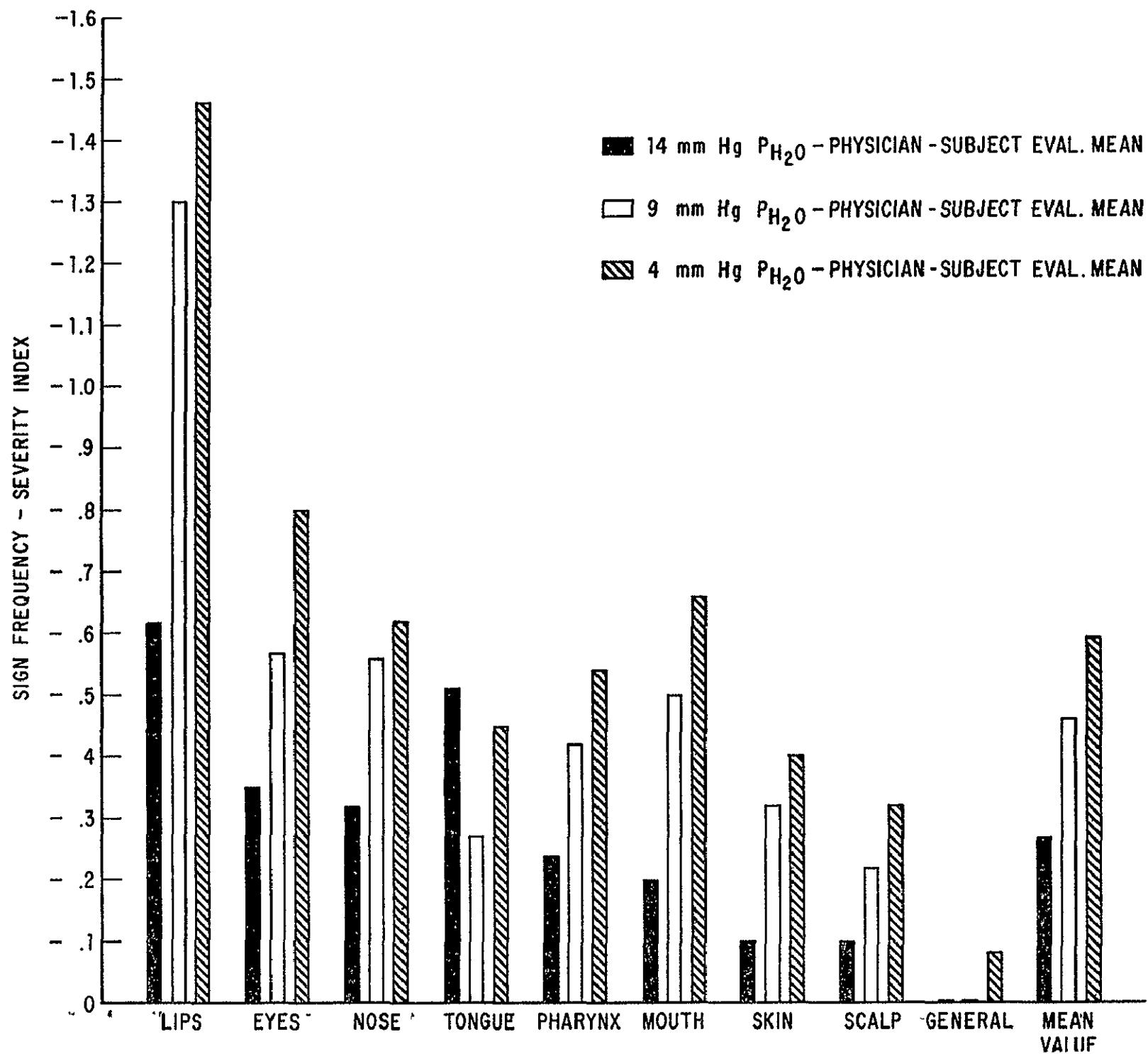


Fig. 45    Frequency-severity of signs related to the environment.  
Effects of  $T_a$  at 700 mm Hg  $P_B$  (matched 24-hr and 48-hr  
experiments).

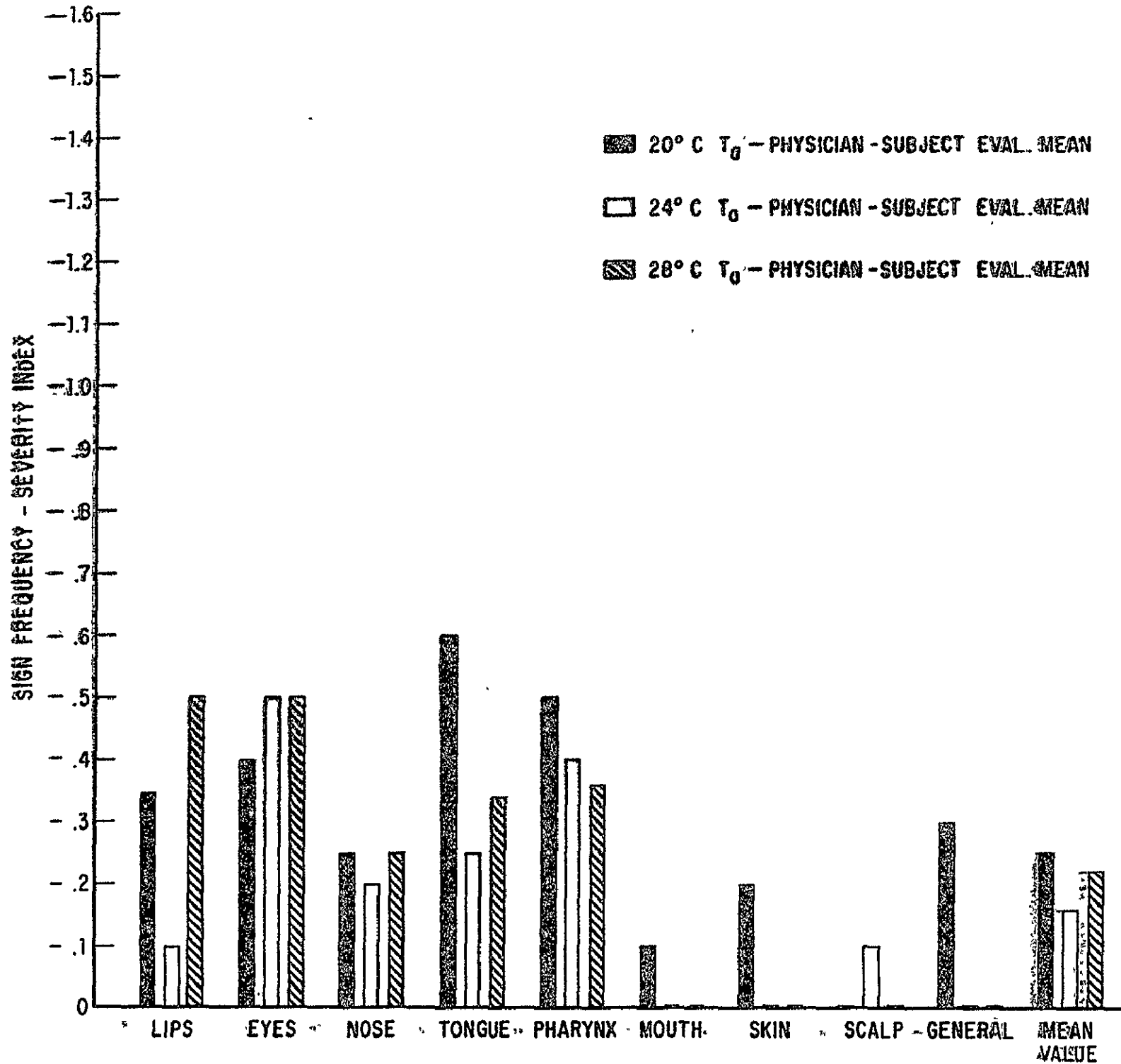


Fig. 46 Frequency-severity of signs related to the environment.  
Effect of gas composition at 258 mm Hg  $P_B$  and 24° C.  $T_a$   
(matched experiments).

5  
⊕

-231-

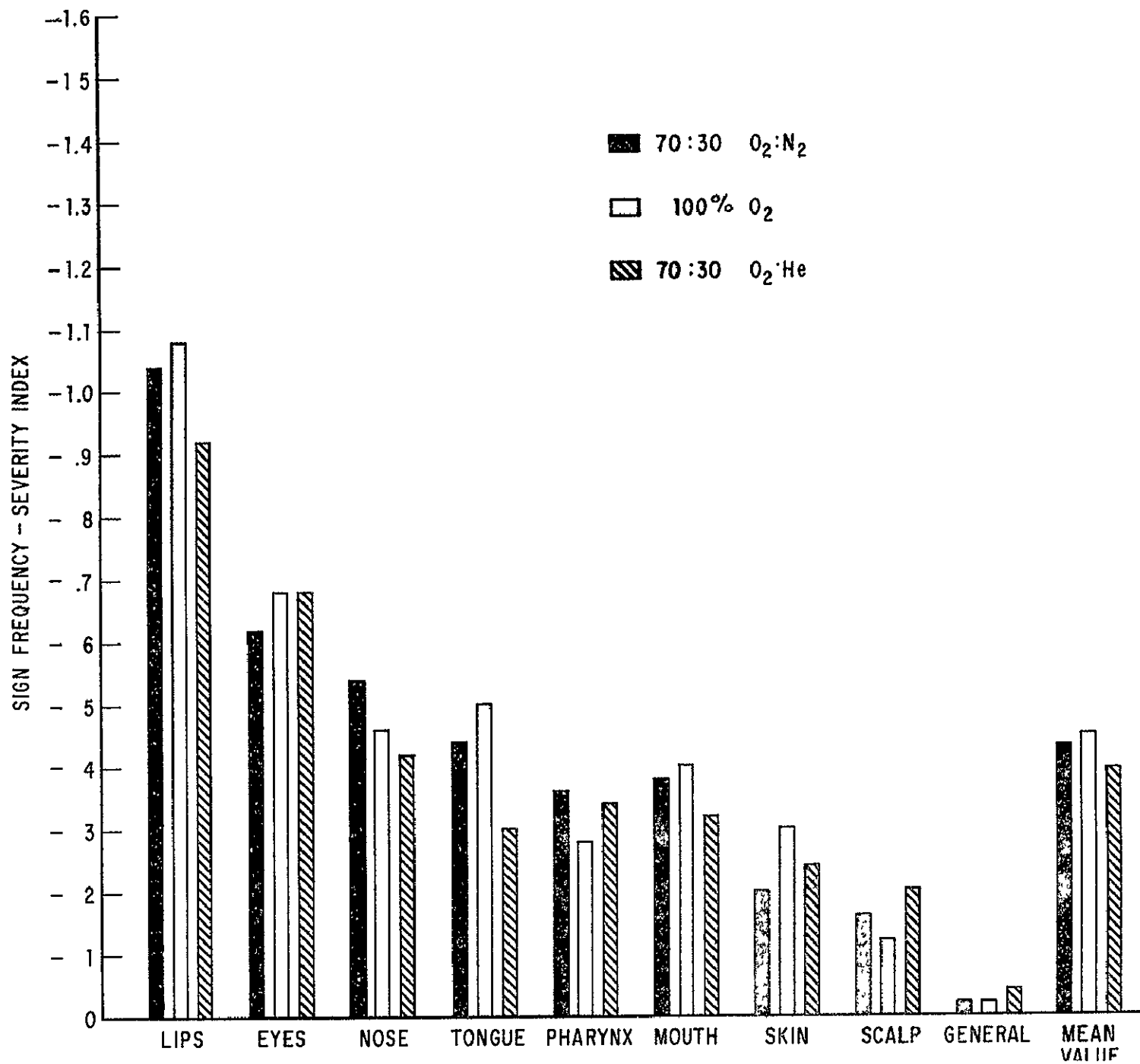


Fig. 47 Relationship of effective wall temperature ( $T_{ew}$ ) to  $T_s$  at varying  $P_B$ , G.C. and  $V$ . (Compare with Fig. 9.)



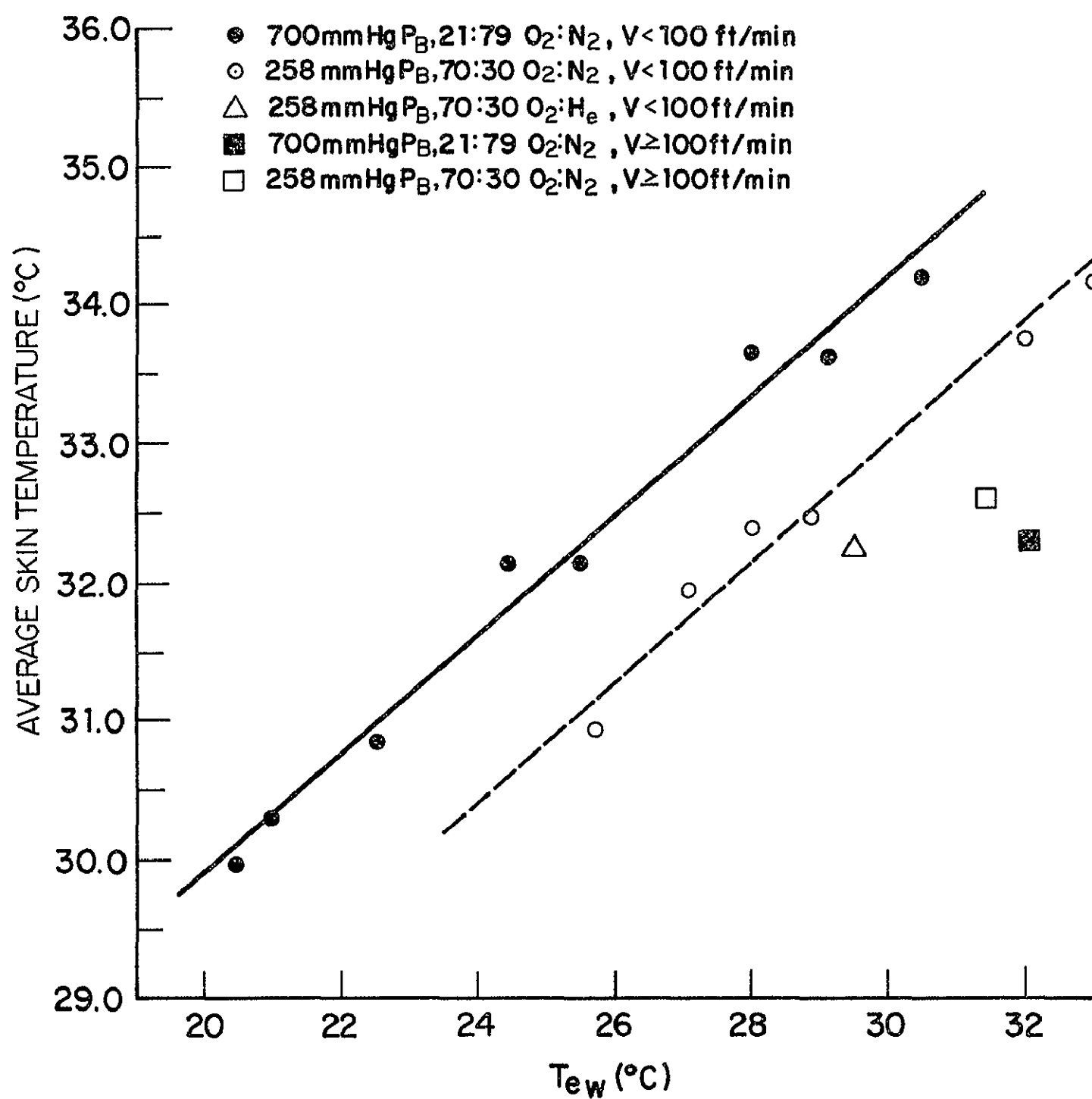


Fig. 48      Comparison of two high-IWL<sub>S</sub> environments (B and C) with a low IWL<sub>S</sub>-environment (A). Increases in IWL<sub>S</sub>, IWL<sub>R</sub>, IWL<sub>T</sub>, and the Sign-Symptom Index for environments B and C are expressed as a percent change over the comparable values for environment A. Note the proportionate increases in IWL<sub>S</sub>, IWL<sub>T</sub>, and the Sign-Symptom Index in environments B and C.

(LOW IWL<sub>S</sub> ENVIRONMENT)(HIGH IWL<sub>S</sub> ENVIRONMENTS)

A. 700mmHg P<sub>B</sub> 14 mmHg P<sub>H2O</sub> 20°C T<sub>a</sub> 50 ft/min V  
 B. 258mmHg P<sub>B</sub> 6.8 mmHg P<sub>H2O</sub> 28°C T<sub>a</sub> 150 ft/min V  
 C. 258mmHg P<sub>B</sub> 4.8 mmHg P<sub>H2O</sub> 28°C T<sub>a</sub> 50 ft/min V

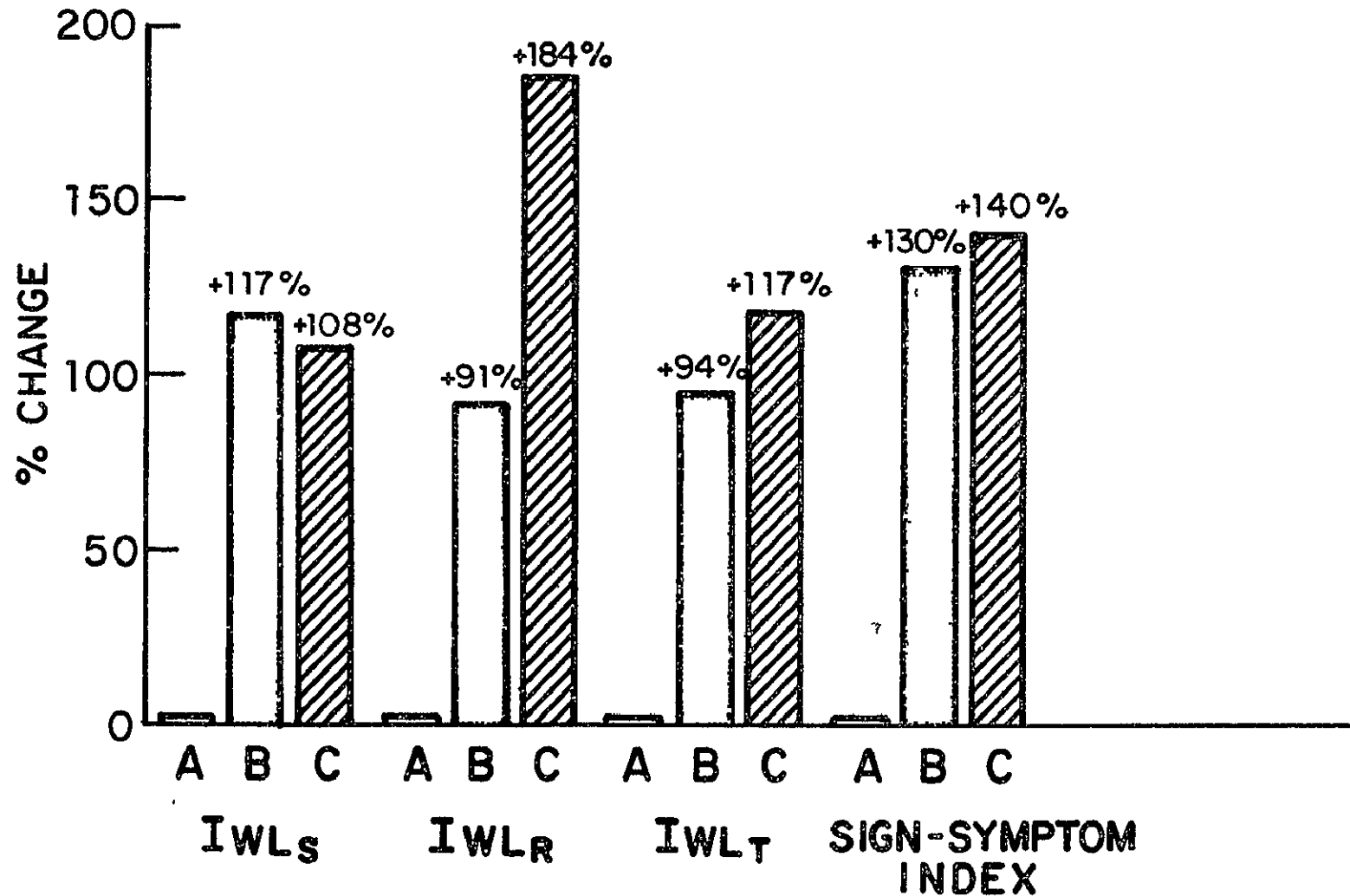
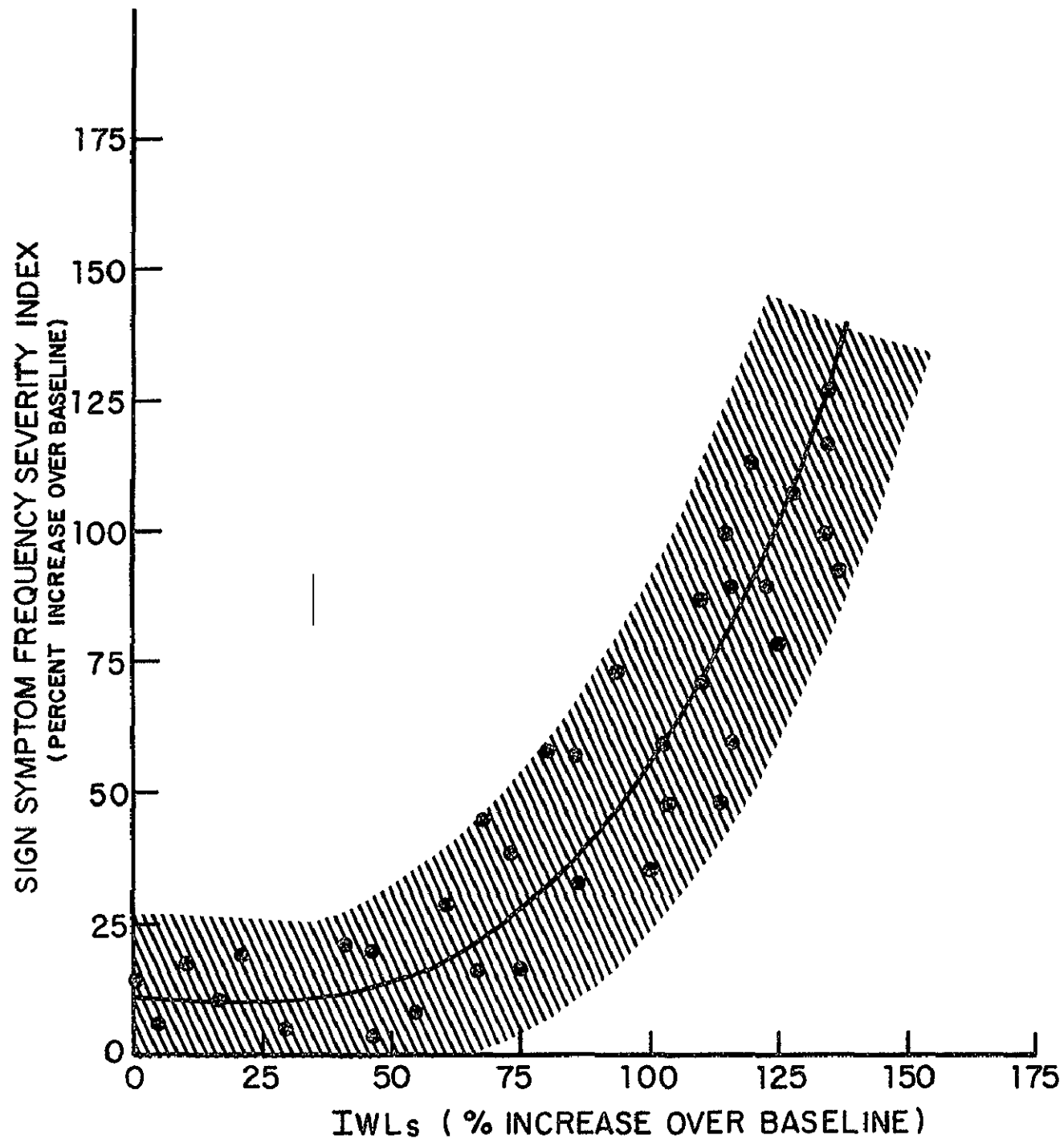


Fig. 49 Relationship of rates of skin insensible water loss to the Sign-Symptom Index. Both parameters are expressed as a percent increase over the baseline values. Note that the Sign-Symptom Index does not begin to increase rapidly until IWL<sub>s</sub> has increased by more than 50% over baseline.

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